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Pathology

956. **Investigations on the Role of the Central Nervous System in Shock Produced by Endotoxin from Gram-negative Microorganisms**
M. H. WEIL, L. D. MACLEAN, W. W. SPINK, and M. B. VISSCHER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **48**, 661–672, Nov., 1956. 5 figs., 26 refs.

It has been shown that a variety of reproducible functional and anatomical disturbances follow the intravenous administration to experimental animals of endotoxin from various species of Gram-negative organisms, and it has been suggested by several investigators that these, particularly the shock and vasomotor collapse, result from a primary action of toxic products on the vasomotor centre. In this paper from the University of Minnesota, Minneapolis, the authors report the results of a re-investigation of the role of the central nervous system in the production of shock induced by endotoxin.

In intact, unanaesthetized dogs the intravenous injection of purified and crude endotoxin from *Brucella melitensis* and *Escherichia coli* caused hyperpnoea, agitation, bloody vomiting and diarrhoea, a progressive fall in the systemic blood pressure, and a transient rise in the portal venous pressure. Coma ensued in 3 hours and death in 4 to 18 hours. At necropsy, severe congestion of the liver and surface epithelial sloughing of large portions of the small intestine were constant findings; in anaesthetized dogs these gastro-intestinal changes were not observed, although the other post-mortem findings were the same. In further experiments on 2 dogs in which the cross-circulation method of Pinner and Klein was used shock and the classic pathological changes were not limited to the animal whose brain was perfused with endotoxin. This result is contrary to previous findings, but it is pointed out that extensive interchange of blood can take place through anastomotic channels within the spinal canal. In other dogs arterial hypotension due to the endotoxins was not prevented by chordotomy, either with or without vagotomy, nor yet by surgical decapitation, and the shock was more rapidly fatal. In studies on cats in which the entire spinal cord was destroyed by pithing, endotoxin still caused a profound fall in the arterial blood pressure, a small rise in portal venous pressure, and the characteristic morphological changes.

The authors conclude that these findings do not support the thesis that the initial manifestations of shock produced by endotoxins are the result of a direct action on the higher nervous centres, although the central nervous system may have an important influence on the subsequent course and lethality of shock after it has been precipitated. *A. Ackroyd*

957. **Reactions of the Single Neurone of the Sensorimotor Cortex after Electrical Stimulation. I. Inhibition and Excitation after a Single Stimulation Applied Directly and Contralaterally.** (Reaktionen einzelner Neurone des senso-motorischen Cortex nach elektrischen Reizen. I. Hemmung und Erregung nach direkten und kontralateralen Einzelreizen)
O. CREUTZFELDT, G. BAUMGARTNER, and L. SCHOEN. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **194**, 597–619, 1956. Bibliography

The experiments here reported from the University of Freiburg im Breisgau were performed on cats which had been prepared as *encéphale isolé*, the present paper dealing only with results of single electrical stimulation of the sensorimotor cortex (later articles will discuss double and serial stimulation). The activation of the neurones was recorded by micropipettes situated extracellularly. The response of the neurones to a single stimulation varied considerably, in some cases even being absent at first, but there was always a constant phase of inhibition lasting from 100 to 400 microseconds. This was followed by a period of secondary activation, during which even those neurones discharged which had proved inactive at first. It was shown that stimuli applied during the phase of inhibition could prolong this phase to double its normal duration. By the use of repeated stimulation, however, the primary discharge was facilitated and the period of inhibition diminished. There was also a second late inhibitory phase occurring after the secondary activation. The same phenomena were observed whether the stimulation was applied to the ipsilateral or to the contralateral corresponding cortical area.

These findings refer to the motor cortex only. In other cortical areas a variety of responses was found. The reaction of the optical cortex, for example, showed a much shorter duration of inhibition and greater secondary activation when the stimulus was applied on the same side, while contralateral application produced inconstant results.

[These are only a few results of the experiments carried out with remarkable technical skill and exactitude in the laboratory of Jung at Freiburg. The inhibitory action of the cortex has for long been postulated theoretically but so far had never been directly demonstrated.]

W. Mayer-Gross

958. **The Protein Levels of Oedema Fluids**
D. J. CROCKETT. *Lancet* [*Lancet*] **2**, 1179–1182, Dec. 8, 1956. 3 figs., 13 refs.

In this communication from the Institute of Clinical Research, Middlesex Hospital, London, the results of determination of the protein content of some 400 samples of oedema fluid from more than 200 patients are reported. The fluid was collected through diminutive Southey-type needles and stored in sealed glass capillary tubes, and the protein content was estimated by an ultramicro-Kjeldahl procedure, with microdiffusion and titration. Six kinds of oedema were specially studied, namely, cardiac, hypoproteinaemic (one of renal and two of hepatic origin), paralytic (mostly hemiplegias), venous, and lymphoedematous, the last named being either idiopathic or secondary to malignant disease or to operations on or irradiation of regional lymph nodes. Cases of doubtful aetiology were excluded.

The fluids in venous, cardiac, and hypoproteinaemic oedema (in descending order of protein content) were found to have low mean protein levels, that is, less than 1 g. per 100 ml., the value being independent of duration of the oedema. (The higher level found in venous oedema is attributed to the change in capillary permeability which is associated with any considerable rise of venous pressure.) In the remaining three categories the levels were higher (1 to 5 g. per 100 ml.), and furthermore tended to rise in a manner proportional to the logarithm of the duration of the oedema; in these types the oedema is attributed to a failure of lymph drainage of tissue-fluid protein. Very high protein levels were found in oedema fluid after a burn and in a case of acute allergic oedema, reaching 6 g. per 100 ml. soon after onset.

It was noted that the protein level was consistently higher in fluid from the arms than in that from the legs, and that the level was higher if the limb was raised, and also after treatment with diuretics. The values for individual cases showed a wide scatter about the mean, except in the cases of hypoproteinaemic oedema and lymphoedema. In a number of cases of chronic oedema of unknown cause in older people the protein levels ranged from 1·0 to 1·5 g. per 100 ml.

Denis Abelson

959. **Paper Electrophoresis of Serum-proteins in Hepatobiliary Disease**
J. A. OWEN and R. F. ROBERTSON. *Lancet* [*Lancet*] **2**, 1125–1129, Dec. 1, 1956. 32 refs.

The value of paper-electrophoretic analysis of serum proteins in hepatic and biliary disease is discussed, with reference to 100 patients examined at Edinburgh Royal Infirmary. The values for albumin and the various globulin fractions in the sera from 34 normal subjects and 21 patients with infective hepatitis, 13 with extrahepatic neoplasm, 22 with stone in the common bile duct, 9 with cholecystitis, 12 with diffuse hepatic fibrosis, 4 with precirrhotic hepatitis, 7 with cardiac cirrhosis, 5 with secondary neoplasm in the liver, 3 with reticulosis in the liver, 2 with acute hepatic necrosis, and 2 with "cholangiolitic cirrhosis" were determined and are expressed as percentages of the total serum protein value. The results, in general, agreed with those of previous investigators.

The authors conclude that paper electrophoresis is not a substitute for the biochemical tests at present in routine use for the assessment of patients with hepatobiliary disease. However, paper-electrophoretic analysis does provide important information regarding (1) the prognosis in infective hepatitis, particularly in cases showing potentially unfavourable clinical features; (2) in confirming the diagnosis in cases of diffuse hepatic fibrosis, especially in differentiation of this condition from secondary hepatic neoplasm in a patient with ascites; and (3) for the preoperative assessment of liver function in patients with extrahepatic biliary obstruction. Paper electrophoresis is of no value in the detection of early impairment of liver function, and is of only occasional value in distinguishing between hepatogenous jaundice and jaundice due to extrahepatic obstruction. In other conditions, such as acute hepatic necrosis, electrophoretic analysis is of interest, but has no practical value.

J. E. Page

960. **Total Exchangeable Potassium in Normal Subjects with Special Reference to Changes with Age**
U. SAGILD. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **8**, 44–50, 1956. 1 fig., 12 refs.

HAEMATOLOGY

961. **The Prothrombin Conversion Ratio**
P. WOLF. *British Journal of Haematology* [*Brit. J. Haemat.*] **2**, 367–374, Oct., 1956. 3 figs., 7 refs.

When plasma is recalcified under standard conditions the rate of thrombin production rises to a maximum during the first 5 minutes; if now excess thromboplastin is added a second maximum production of thrombin occurs after a further 5½ minutes. The author, working at the Lister Institute, London, has used the ratio of these two maxima as a measurement of prothrombin conversion. It has the advantage over the thrombin generation test of being almost independent of the amount of prothrombin present.

By substituting for the thrombin-containing solution in the determination of the prothrombin conversion ratio a mixture of 0·1 ml. of centrifuged plasma, 0·7 ml. of "veronal" buffer, and 0·2 ml. of platelet suspension, the effect of the platelet suspension can be measured. Instead of the platelet suspension the platelet substitute of Bell and Alton was found to be a stable and consistent reagent. In blood stored at 4° C. the prothrombin conversion ratio rose to a maximum in 18 hours, but this change was prevented by removal of platelets. The optimum platelet concentration was found to be 320,000 per c.mm.

The author suggests that the observed inhibitory effect of high concentrations of platelets on prothrombin conversion may play some part in bleeding diseases associated with a very high platelet count.

Marjorie Le Vay

962. **Lipid Extracts of Platelets and Brain as Substitutes for Platelets in Coagulation Tests**
P. WOLF. *British Journal of Haematology* [*Brit. J. Haemat.*] **2**, 375–385, Oct., 1956. 2 figs., 25 refs.

In this study the author has compared the effect of adding fresh and old platelet suspensions, ether extracts of platelets, and chloroform extracts of brain lipids to normal and haemophilic plasma when estimating the prothrombin conversion ratio [see Abstract 961]. The ratio was found to be increased by increasing the concentration of platelets, and similarly of extracts, and an inhibitory effect with high concentrations of any of these reagents was found to be an antithromboplastin effect. Neither platelets nor extracts influenced the thrombin–fibrinogen reaction. The only important difference shown was that platelet suspensions had an anti-heparin effect, in the presence of plasma only, which was not possessed by either of the extracts. *Marjorie Le Vay*

963. **Assay of Antihaemophilic Factor Using the Prothrombin Conversion Ratio**
P. WOLF. *British Journal of Haematology* [*Brit. J. Haemat.*] **2**, 386–396, Oct., 1956. 3 figs., 13 refs.

In this paper from the Lister Institute, London, the author describes a method of assay of the antihaemophilic factor (A.H.F.), in which he uses an artificial haemophilic substrate prepared by ether fractionation and freeze-drying of normal plasma, this procedure removing most of the antihaemophilic activity. By comparing the values for the prothrombin conversion ratio [see Abstract 961] obtained with this substrate, first when dilute standard plasma is added and then when dilute test plasma is added, a value for the A.H.F. present is obtained. It is pointed out that allowance has to be made for the fact that if the A.H.F. content is low and the fibrinogen content high appreciable amounts of thrombin are absorbed on to the clot during the test.

Samples of platelet-free plasma from 12 haemophiliacs were examined; in all but one the A.H.F. value was below 3 units per ml. In 200 samples of normal plasma assayed values ranging from 8 to 18 (mean 12·5) units were found. Reasonable agreement with the thrombin-generation and thromboplastin-generation tests was obtained, and the assay was much simpler than these to perform. By reference to a standard plasma the results of all assays may be made comparable. Further, the method of assay can be slightly modified to provide a simple means of determining the effect of specific therapy on the haemophilic state. *Marjorie Le Vay*

964. **Observations on the Sickling Phenomenon and on the Distribution of Different Haemoglobin Types in Erythrocyte Populations**
A. C. ALLISON. *Clinical Science* [*Clin. Sci.*] **15**, 497–510, Nov., 1956. 5 figs., 31 refs.

Working at the M.R.C. Unit for Research in Cell Metabolism, University of Oxford, the author has studied the behaviour of sickle cells *in vitro* and has correlated his observations with the known clinical features of sickle-cell disease. When blood from carriers of the sickle-cell trait was compared with that of patients with sickle-cell anaemia a large proportion of the patients' erythrocytes (which contain more of the abnormal haemoglobin) showed sickling when the oxygen tension was maintained at about 30 mm. Hg, whereas virtually no sickling occurred in the erythrocytes of the sickle-cell trait carriers until the oxygen tension fell well below this level. It was confirmed that sickling is inhibited at low temperatures (1° to 4° C.), and shown that the critical temperature was 18° C., a further increase in the number of sickle cells being seen when the temperature was raised to 37° C. The author also demonstrated that there is a distinct time factor concerned in the sickling phenomenon, for measurement of the interval between de-oxygenation and the first appearance of sickling showed that this period was of the order of 3 minutes. Lastly, by inducing partial sickling of blood samples and making use of the fact that sickle cells are more resistant to hypotonic saline than non-sickled cells, the author demonstrated that the proportion of sickle-cell haemoglobin in the cells of a carrier of the sickle-cell trait does not seem to be uniform.

It is concluded that the partial oxygen tension in most tissues is low enough to induce sickling in a significant proportion of erythrocytes of persons with sickle-cell anaemia, but not in those of trait carriers. Since sickling takes rather longer than 15 seconds to complete, most cells, even in patients with sickle-cell anaemia, will be re-oxygenated before they can become sickled. If, however, re-oxygenation is impeded for a time extending to minutes rather than seconds considerable intravascular sickling is to be expected. *H. Lehmann*

MORBID ANATOMY AND CYTOLOGY

965. **Histological Findings in the Choroid Plexus in Infantile Hypersecretory Hydrocephalus.** (Histologische Befunde an den Plexus chorioides bei frühkindlichem Hydrocephalus hypersecretorius)
O. E. LUND. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **195**, 205–218, 1956. 6 figs., bibliography.

The material for this study was obtained by biopsy at the University Neurosurgical Clinic, Bonn, during the course of operations on the ventricles of the brain for the relief of infantile hydrocephalus. Removal of the choroid plexus from the lateral ventricles was effected in 10 cases from one ventricle and in 2 cases from both sides. The ages of the 12 patients (6 boys and 6 girls) ranged from 2 to 24 months. In only one case was the hydrocephalus observed at the time of birth, in 5 it became apparent between one and 20 weeks after normal birth, and in the remaining 6 the hydrocephalus occurred during or following meningitis.

Histologically, the outstanding lesion in the choroid plexus, observed in 10 out of the 12 cases, was a striking variation in the shape of the epithelial cells lining the plexus. Instead of the normal cubical epithelium most of the cells were of high cylindrical form, and had long narrow nuclei, rich in chromatin, instead of rounded, loose nuclei. The distribution of these abnormal cells

was very variable—thus in some parts of one preparation all the cells would be of this type, while in others they mingled with the normal cubical form. [A particularly good illustration of this transition from a normal to abnormal type of cell is shown in one of the photomicrographs which accompany the text.] Another abnormal feature was the presence of large vacuoles at the apices of the cells. These vacuoles occurred in both the normal cubical and abnormal cylindrical forms of epithelium. In 8 cases an increase in the number and size of the blood vessels was found. The diameter of some of the vessels was as much as five times that of the vessels in a normal choroid plexus. These very large vessels were usually distended with blood and occasionally surrounded by inflammatory cells; their walls were thin, and they appeared to be not true blood vessels, but rather angiomatous malformations.

The author regards the variation in shape of the cells of the lining of the choroid plexus as the essential lesion in infantile hydrocephalus. Examination of the choroid plexus of a number of human embryos showed that the cells lining the plexus were of the same high, cylindrical form as in the cases of hydrocephalus. He therefore concludes that the lesion in hydrocephalus is due to failure of the embryonic cells to differentiate, and that any associated inflammatory process present is of secondary importance. *Ruby O. Stern*

966. **The Macroscopic Anatomy of Pulmonary Emphysema**

K. H. McLEAN. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **5**, 73–88, May, 1956 [received Sept., 1956]. 14 figs., 33 refs.

The aetiology of emphysema is not known, and much confusion results from the use of such terms as "compensatory" and "senile", which imply *a priori* hypotheses. Difficulty also results from the fact that the condition is always advanced before clinical changes become apparent. The study of the morphology provides the only information on the early stages, and in this paper from the University of Melbourne the author suggests the following classification, which is purely morphological.

(1) *Localized Emphysema.* (*a*) Lesions clearly related to anatomical units, often associated with bronchiectasis, scars, and bullae. (*b*) Lesions apparently unrelated to anatomical units.

(2) *Generalized Emphysema.* (*a*) Without localized accentuation. (*b*) With local accentuation. Whereas some cases of generalized emphysema have emphysema of the localized type superadded, some cases of extensive emphysema are merely extreme forms of 1*a*, with multiple lesions of the localized type. Most cases of generalized emphysema arise from the multiplication and extension of focal lesions (the centrilobular lesions of Gough). If searched for, one or two such lesions may be found in normal lungs. This lesion is often, but not necessarily, associated with pigmentation. True generalized emphysema occurs in two forms: (i) focal (centrilobular), and (ii) diffuse (with loss of lobular pattern). In all cases emphysema is associated with inflammatory changes, but whether as cause or effect is still unsettled.

The present paper is based on the study of material from 180 cases collected from various sources, but since this material was highly selected the numbers of different types examined gives no true indication of their incidence. A separate investigation of 2,000 consecutive necropsies performed at the Royal Melbourne Hospital showed that chronic bronchitis and emphysema was regarded as the cause of death in only 2·6%, British figures being considerably higher "as might be expected on climatic consideration". But subclinical emphysema was at least three times as common as clinical emphysema, and some degree of the generalized condition is to be expected in at least 25% of necropsies. *D. M. Pryce*

967. **Chondrosarcoma, a Surgical and Pathological Problem. Review of 212 Cases**

D. C. DAHLIN and E. D. HENDERSON. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **38-A**, 1025–1038, Oct., 1956. 11 figs., 10 refs.

An account is presented of the clinical and pathological findings in 212 cases of chondrosarcoma of the trunk and limbs seen at the Mayo Clinic between 1905 and 1955. Over this period these tumours formed less than 10% of the pathologically verified primary bone tumours encountered at the Clinic. Males were twice as frequently affected as females. In the majority of cases the tumour did not develop until adult life (in 101 cases between ages 40 and 59), and the bones most commonly involved were those of the trunk (pelvic girdle and ribs) and the upper ends of the femur and humerus. There was a strikingly low incidence (4 cases) of malignant cartilaginous tumours in the peripheral portions of the extremities.

Pain and swelling were the usual presenting complaints, and these had often been present for several years before advice was sought. The tumours were usually of slow growth, but the authors stress the likelihood, in inadequately treated cases, of repeated recurrences leading ultimately to death. Metastasis occurred in less than 10% of cases, and when it did almost invariably involved the lungs. Important radiological features were destruction of bone and mottled calcification at the involved site.

The importance of biopsy examination in the investigation of these cases is stressed; adequate material must be examined so that chondrosarcoma can be distinguished from benign chondroma, osteochondroma, chondromyxoid fibroma, benign chondroblastoma, and from osteogenic sarcoma with conspicuous cartilaginous differentiation. The tumours in this series were classed histologically into three grades on the basis of their cytological appearances. There was some correlation between the microscopical evidence of cellular activity and the subsequent clinical behaviour of the tumour and hence the prognosis. Adequate surgical resection is the basis of treatment, but the ease with which chondrosarcoma implants itself locally in surgical wounds—including biopsy wounds—is a major problem in the management of these cases. *H. A. Sissons*

Microbiology and Parasitology

968. **Electron Microscopy of Trachoma Virus in Section**
Y. MITSUI and A. SUZUKI. *A.M.A. Archives of Ophthalmology* [*A.M.A. Arch. Ophthal.*] **56**, 429–448, Sept., 1956. 29 figs., 5 refs.

This paper, which contains some striking photomicrographs and comes from the University Medical School, Kumamoto, Japan, reports a study by electron microscopy of the trachoma virus as seen in tissue sections. Paraffin sections for which Giemsa, haematoxylin, eosin, and other stains had been used were also studied. Virus inclusion bodies were stained by haematoxylin but tended to be discoloured by eosin. " Elementary-body inclusions " were seen more frequently than pure initial-body inclusions, except in the acute stage of the disease. When Giemsa stain was used inclusion bodies were often found embedded in an amorphous ground substance, which also stained with iodine. In sections, virus inclusion bodies must be differentiated from mast-cell granules.

As seen by the electron microscope the virus inclusion bodies of trachoma are not uniform in structure. The morphology of these bodies is described; the authors have no doubt that the epithelial inclusion body in trachoma is the actual trachoma virus colony. They compare the appearances under the electron microscope with those under the light microscope. No virus inclusion bodies or virus-like structures were seen in the subepithelial tissues of conjunctival biopsy specimens.

The authors' findings are not opposed to those generally held concerning the life cycle of the trachoma virus. However, certain other features observed by the authors, and visible in the photomicrographs, lead them to consider the possibility of a " vegetative form " in the life cycle of the trachoma virus. *W. G Henderson*

969. **Trial of Phage Antiserum as an Aid in the Bacteriological Diagnosis of Brucellosis in Man.** (Опыт применения антифаговой сыворотки в целях улучшения бактериологической диагностики бруцеллеза у людей)
A. S. FOMICHEVA, V. S. URALEVA, and N. A. CHERNENKOVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 57–62, No. 10, Oct., 1956. 2 figs., 10 refs.

In studies carried out at the Institute of Public Health, Rostov-on-Don, U.S.S.R., the authors, having available an antiserum against *Brucella* phage, added 0·5 ml. of this antiserum to 70 ml. of nutrient broth at *p*H 6·9, into which 1 ml. of blood from patients suspected of having brucellosis was inoculated for culturing; simultaneously, as a control, 1 ml. of blood from each patient was inoculated into 70 ml. of broth not containing phage antiserum. Further, two nutrient agar plates were inoculated with a few drops of blood from the same patients, the plates dried in the incubator in the usual way, and after 20 minutes 0·1 ml. of phage antiserum was spread evenly over the surface of one plate, the other serving as a control. Every 6 or 7 days subcultures were made from the blood cultures.

In all, 145 such tests were carried out on 80 patients. From the blood of those suffering from brucellosis the number of positive cultures obtained on media with phage antiserum was roughly 90% greater than on media without such antiserum. Isolation of *Brucella* was most frequent between the third and sixth months of illness. Growth occurred between 1 and 21 days earlier in media containing the phage antiserum. *K. Zinnemann*

970. **Immunization of Children by the Feeding of Living Attenuated Type I and Type II Poliomyelitis Virus and the Intramuscular Injection of Immune Serum Globulin**
H. KOPROWSKI, T. W. NORTON, G. A. JERVIS, J. STOKES, E. L. MCGEE, and D. J. NELSEN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 378–388, Oct., 1956. 3 figs., 10 refs.

In the investigation herein described various amounts of the rodent-adapted Type-I SM strain of poliomyelitis virus, either alone or with the rodent-adapted non-cytopathogenic Type-II TN strain, were given by mouth in milk or gelatin capsules simultaneously with intramuscular injection of human immune serum globulin to 20 children aged 6 to 12 years who lacked antibody to the type of virus administered. The dosage of immune globulin was 0·15 ml. per lb. body weight (0·33 ml. per kg.). None of the children showed any clinical signs of illness, and injection of the immune serum globulin at the same time as administration of the virus had no effect on either the multiplication of the virus in the intestinal tract or the antibody response.

Type-I poliomyelitis virus was excreted in the stools of all the children for varying periods up to 171 days, but in no regular or established pattern. Type-II virus, on the other hand, was not excreted by any of the 12 children to whom it was administered. Calomel, given in a dosage of 0·05 g. daily with the object of suppressing virus excretion, had no definite effect, although the stools of all except one of the patients given the drug within 10 days of administration of the virus became virus-free within a short time.

The antibody titre could not be correlated with the duration of the carrier state. There was a significant rise in neutralizing antibody titre to Type-I virus in all the children, but in some of those given Type-II no rise in neutralizing antibody titre to this virus type was observed. The antibody titre to Type-I virus was the same whether the virus was ingested in a gelatin capsule or in milk. Culture of throat swabs from all these children proved negative. *A. Ackroyd*

971. **Present Status of Attenuated Live-virus Poliomyelitis Vaccine**
A. B. SABIN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 1589–1596, Dec. 29, 1956. 2 figs., 21 refs.

Pharmacology

972. **The Analgesic Properties of Numorphan (14-Hydroxy Dihydromorphinone). A New Synthetic Narcotic**
A. COBLENTZ and H. R. BIERMAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 694–698, Oct. 11, 1956. 4 figs., 2 refs.

At the City of Hope Medical Center, Duarte, California, 200 patients suffering from neoplastic disease were treated with " numorphan ", 51 receiving it (together with atropine) as preoperative medication, 95 postoperatively, and the remaining 54 for comparison with other narcotics in the relief of severe pain. Numorphan (14-hydroxy-dihydromorphinone) is a synthetically prepared derivative of morphine. On the basis of a double-blind trial it was estimated that 2 mg. of numorphan was equivalent to 16 mg. of morphine sulphate in analgesic effect. No untoward side-effects were noted following single doses up to 10 mg., and constipation was notably absent. In one debilitated patient a dose of 5 mg. of numorphan produced severe respiratory depression, which however was readily reversed by administration of nalorphine. From this limited experience it is thought that the danger of addiction appears to be as great with numorphan as with morphine.

P. Mestitz

973. **Chlorpromazine and Spasticity.** (Chlorpromazin und Spastizität)
H. D. HENATSCH and D. H. INGVAR. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **195**, 77–93, 1956. 8 figs., 32 refs.

At the Nobel Institute of Neurophysiology, Stockholm, the authors have studied the effects of chlorpromazine on spinal motor activity in experimentally produced spastic states in cats, employing the methods and concepts of Granit and co-workers.

The results were as follows. In cats rendered decerebrate by intracollicular section (" gamma cats ") intravenous chlorpromazine in doses of 0·5 to 2·5 mg. per kg. body weight rapidly changed the decerebrate rigidity into a flaccid state lasting many hours. By recording impulses from anterior root fibres it was shown that chlorpromazine blocks the tonic activity of the " gamma " motor neurones. Stimulation of the brainstem reticular formation, skin, or pinna, which normally causes an increase in the activity of " gamma " motor neurones, no longer had this effect.

After de-efferentation chlorpromazine did not alter the response of isolated muscle spindles to muscle stretching, nor was the " post-tetanic potentiation " state in the monosynaptic reflex of decerebrate or spinal preparations appreciably altered by chlorpromazine. However, in isolated fibres of " alpha " motor neurones there was a complete suppression of potentiation of their responses to muscle stretching. In cats decerebrated by the " anaemic " method (" alpha cats ") chlorpromazine had no effect on the severe rigidity. Recordings of anterior root responses showed that chlorpromazine reduces the activity of the " gamma " motor neurones, but produces a sustained increase in the response of the " alpha " motor neurones to muscle stretching.

The authors conclude that chlorpromazine influences spinal motor functions and spastic states because of its action on the supraspinal control of the " gamma " motor neurones. The drug also has an inhibitory action on the reticular system of the mesencephalon and medulla.

F. Letemendia

974. **Lidocaine in Cardiac Resuscitation from Ventricular Fibrillation**
N. L. CARDEN and J. E. STEINHAUS. *Circulation Research* [*Circulat. Res.*] **4**, 680–683, Nov., 1956. 1 fig., 4 refs.

In this study of the effect of lidocaine (lignocaine) on ventricular fibrillation, carried out at Wisconsin Medical School, Madison, 23 dogs were anaesthetized with pentobarbitone, the chest opened, and ventricular fibrillation induced by means of temporary occlusion of the circumflex artery, the electrocardiogram being recorded and the blood pressure measured with a strain gauge. Massage was started one or 2 minutes after the onset of fibrillation, and when adequate circulation was established 15 mg. of lignocaine per kg. body weight was injected into the left ventricle, the massage being continued for 30 to 60 seconds with the aorta occluded to ensure distribution of the drug in the coronary vessels, and further massage given if necessary until an organized beat was established. Then 40 μg. of noradrenaline was injected into the left ventricle and a solution of noradrenaline (40 μg. per ml.) infused intravenously as necessary to maintain blood pressure. Dextran or 5% dextrose was also given to compensate for any loss of blood.

Of the 23 dogs treated in this manner, regular cardiac contraction was maintained in 21 for at least one hour after cessation of fibrillation. The time required to establish a regular contraction varied from 2 to 27 minutes (mean 7 minutes) after the onset of arrhythmia.

To determine whether complete recovery could be obtained with lignocaine the chests of the 21 resuscitated dogs were surgically closed and they were allowed to recover; 16 of these dogs lived for at least 24 hours, and of the 5 that died, in only one was death due to the recurrence of fibrillation. In a further group of dogs whose body temperature was lowered to 28° to 30° C. before instituting fibrillation the survival rate was less good, only 5 living for 24 hours after resuscitation.

P. A. Nasmyth

975. **Dioctyl Sodium Sulphosuccinate in the Treatment of Constipation**
J. RENDLE-SHORT. *Lancet* [*Lancet*] **2**, 1189–1190, Dec. 8, 1956. 2 refs.

Chemotherapy

976. **The Intracellular Activation of Pyrazinamide and Nicotinamide**
G. B. MACKANESS. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **74**, 718–728, Nov., 1956. 1 fig., 21 refs.

The antibacterial activity of pyrazinamide and nicotinamide against tubercle bacilli, Strain H37Rv, grown in isolated rabbit monocytes *in vitro* has been investigated at the Australian National University, Canberra. Fluid cultures of rabbit monocytes containing ingested living tubercle bacilli were maintained in centre-well culture chambers in nutrient media to which varying amounts of pyrazinamide or nicotinamide (up to 50 μg. per ml.) were added. The percentage of infected monocytes, the average number of bacilli per monocyte, and the coefficient of increase in the number of bacteria were calculated for control cultures and for cultures treated with varying concentrations of drug.

It was shown that although pyrazinamide and nicotinamide at concentrations of 500 μg. per ml. did not inhibit the growth of tubercle bacilli under conventional conditions in " tween "–albumin medium, 12·5 μg. of either drug per ml. almost completely inhibited the growth of intracellular tubercle bacilli. Compared with isoniazid, pyrazinamide had only a slow bactericidal effect upon intracellular tubercle bacilli; when combined with isoniazid, pyrazinamide caused an apparent increase in the bactericidal effect of the former. The discrepancy between the antituberculous activity of pyrazinamide *in vivo* and *in vitro* (where it is very low) is discussed. It is possible that it may depend on the *p*H of the ambient medium. *J. E. Page*

977. **Sulfamethoxypyridazine (Kynex): a New Long-acting Sulfonamide**
W. P. BOGER, C. S. STRICKLAND, and J. M. GYLFE. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **3**, 378–387, Nov., 1956. 4 figs., 7 refs.

A new antibacterial sulfonamide, sulfamethoxypyridazine, has been studied in 67 patients and administered to an additional 35 patients in doses ranging from 1 to 4 g. The plasma concentrations following the oral administration of single 1- and 2-g. doses of the drug have been determined. The drug is rapidly absorbed from the gastrointestinal tract, and therapeutically significant plasma concentrations are promptly achieved and are maintained for many hours. The drug can be measured in the plasma for as long as 168 hours following a single 2-g. dose. Sulfamethoxypyridazine is slowly excreted into the urine both as free and acetylated compound. The insolubility of the acetylated form and its appearance in quantity in the urine is a characteristic of the drug that will require care in its use. The diffusion of sulfamethoxypyridazine into the cerebrospinal fluid occurs to a greater extent than has been our experience with some other commonly employed sulfonamides. The antibacterial and pharmacologic properties of sulfamethoxypyridazine are such as to give every anticipation of dosage schedules that will be therapeutically effective and, at the same time, distinctive and unique among presently available sulfonamide drugs.—[Authors' summary.]

ANTIBIOTICS

978. **Novobiocin for Infections Due to *Micrococcus pyogenes***
W. J. MARTIN, F. R. HEILMAN, D. R. NICHOLS, W. E. WELLMAN, and J. E. GERACI. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 1150–1153, Nov. 17, 1956. 8 refs.

Novobiocin, an antibiotic shown to be specially active against staphylococci, was administered by mouth to 53 patients who had been admitted to the Mayo Clinic with infections caused by these organisms. Dosages were as follows: for infections of moderate severity, 500 mg. 6-hourly; for less serious infections, the same dose every 8 or 12 hours; and for minor infections, 250 mg. every 6 to 8 hours. In very young children 100 mg. was given by mouth in syrup or in a special capsule. Results stated to be as satisfactory as those expected with other antibiotics were obtained in 48 cases. Of 7 patients with staphylococcal bacteriaemia, the blood stream was sterilized in 5. A satisfactory clinical result was obtained in 20 of 22 cases of infection of the skeletal system and soft tissues, but other treatment, including surgery, was also given. In 13 cases of staphylococcal enterocolitis, oral administration of novobiocin restored the flora of the stools to normal in 24 to 72 hours. As regards toxicity, mild gastro-intestinal upset (cramps, nausea, and liquid stools) was noted in a number of cases, but did not require discontinuance of therapy. Allergic dermatitis occurred in 5 of the 53 cases. There was no apparent renal or haematopoietic damage. The virtual restriction of the use of novobiocin to resistant staphylococcal infections is suggested. *Norval Taylor*

979. **Two New Antibiotics. Antibacterial Activity of Novobiocin and Vancomycin**
R. W. FAIRBROTHER and B. L. WILLIAMS. *Lancet* [*Lancet*] **2**, 1177–1179, Dec. 8, 1956. 7 refs.

The tendency of many organisms, especially *Staphylococcus aureus*, to show resistance to established antibiotics has made the introduction of new products a matter of considerable importance. A study of the activity *in vitro* of vancomycin and novobiocin in order to assess their clinical potentialities is reported from the Royal Infirmary, Manchester. Tests to determine the sensitivity of the common pathogenic bacteria indicated that both vancomycin and novobiocin were

active against most Gram-positive cocci. The range of antibacterial activity of vancomycin was similar to that of penicillin, erythromycin, and bacitracin; thus this antibiotic should be especially valuable in the treatment of infections caused by penicillin-resistant staphylococci. Novobiocin should also be of value against penicillin-resistant strains of *Staph. aureus*, although the results of sensitivity tests with this substance *in vitro* were considerably influenced by such factors as the strength of the inoculum and the type and *p*H of the medium used. Novobiocin-resistant strains of *Staph. aureus* have already been isolated in the U.S.A. Little or no activity against the Gram-negative bacilli usually associated with urinary infections was found with either antibiotic.

L. A. Elson

980. **Blood Levels after Oral Penicillin V (Free Acid) in Children**

E. J. Holborow, E. G. L. Bywaters, and G. D. Johnson. *British Medical Journal* [*Brit. med. J.*] **2**, 1338–1340, Dec. 8, 1956. 3 figs., 7 refs.

A study of the blood levels following oral administration of 120 mg. of phenoxymethylpenicillin (free acid) and 200,000 units of benzylpenicillin in 6 children convalescent from rheumatic fever is reported from the Canadian Red Cross Memorial Hospital, Taplow, Buckinghamshire. Penicillin was given half an hour or one hour before lunch and half an hour after lunch, and blood levels were determined one hour and 3 and 5 hours after administration, a strain of group-A haemolytic streptococci (Type 4) being used.

With either form of penicillin considerable differences were found between patients in the penicillin levels in blood taken at the same time after administration, this variation being less marked at 3 and 5 hours than at one hour. The blood level at one hour tended to be higher if the drug was given after food than if it was given before, this being true for both forms of penicillin. There was some delay in absorption of phenoxymethylpenicillin, 8 out of 20 one-hour blood samples showing no detectable penicillin levels. At 3 and 5 hours after administration the blood levels of phenoxymethylpenicillin were significantly higher than those of benzylpenicillin; again, the levels were higher when the drug was given after food. *Gerald Sandler*

981. **Oral Administration of Penicillin. With a Note on Methods of Assay**

L. Henry, G. White, and M. J. Meynell. *British Medical Journal* [*Brit. med. J.*] **1**, 17–19, Jan. 5, 1957. 11 refs.

A comparative investigation is reported from the General Hospital, Birmingham, of the serum levels and urinary excretion of penicillin following administration of phenoxymethylpenicillin and benzathine penicillin by mouth and crystalline benzylpenicillin and procaine penicillin by intramuscular injection, 200,000 units of each preparation being given. The 6 subjects included in the investigation received each preparation in turn before meals. Specimens of blood were withdrawn after intervals of 30 minutes and one, 2, 3, and 5 hours, except after administration of procaine penicillin, when the intervals were 30 minutes, one hour, and 2, 6, and 24 hours; a 24-hour specimen of urine was also collected. Serum penicillin levels were assayed by both the serial broth-dilution method with *Staphylococcus aureus* (Oxford strain) and the plate method with *Sarcina lutea*, but the latter method only was used for assay of urinary excretion because of the possibility of contamination. These techniques are described in some detail, including the composition of culture media and the assay procedure. It is pointed out that the plate method with *Sarcina lutea* is most reliable, having an accuracy within 5%, whereas the *Staph. aureus* method, although simpler to carry out, has an inherent accuracy of only 50%, and in fact in 44 out of 120 instances the readings were not even within this range of accuracy.

Penicillin given parenterally was well absorbed; with the crystalline form there was a high blood level for a short time, which, however, fell to less than 0·1 unit per ml. after 3 hours; with procaine penicillin the blood level was lower but was maintained for a longer time (0·35 unit per ml. at 6 hours). With parenteral administration 75% of the dose was recovered from the urine in 24 hours. When phenoxymethylpenicillin was given by mouth there was an adequate blood level for over 3 hours, although only 30% of the dose was recovered in a 24-hour specimen of urine. Benzathine penicillin by mouth was unsatisfactory, a therapeutic blood level lasting only for one hour and only 5 to 10% of the dose being recovered in a 24-hour specimen of urine.

Gerald Sandler

982. **Antibiotic Combinations. Antistreptococcal and Antistaphylococcal Activity of Plasma of Normal Subjects after Ingestion of Erythromycin or Penicillin or Both**

W. F. Jones and M. Finland. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 1019–1024, Nov. 29, 1956. 4 figs., 7 refs.

Different preparations of erythromycin, alone or in combinations with penicillin V [phenoxymethylpenicillin] or penicillin G [benzylpenicillin], and also the two forms of penicillin alone, were given in comparable total amounts, and the activity of all these preparations compared on the basis of the antistreptococcal and antistaphylococcal activity that they produced in the plasma of normal subjects. Many differences were revealed, some of which suggested the possibility that erythromycin and penicillin V were manifesting antagonistic action. Further study of the data, however, revealed differences in the absorption of the various dosage forms that, together with previously demonstrated differences in activity of oral preparations of penicillins V and G, might be responsible for most of the difference in activity observed when all these agents were used singly or in combinations of erythromycin with penicillin.—[Authors' summary.]

983. ***In-vitro* Response of Enteropathogenic *Escherichia coli* to Various Antibiotics**

W. I. Metzger and C. J. Jenkins. *Pediatrics* [*Pediatrics*] **18**, 929–934, Dec., 1956. 6 figs., 7 refs.

Infectious Diseases

984. **Nonbacterial Regional Lymphadenitis ("Cat-scratch Fever"). Evaluation of Surgical Treatment**
W. T. SMALL and R. C. SNIFFEN. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 1029–1033, Nov. 29, 1956. 3 figs., 5 refs.

During a period of one year 7 patients believed to be suffering from cat-scratch fever were admitted to the Memorial Hospital, Worcester, Massachusetts. They ranged in age from 4 to 16 years. The intradermal test was positive in 6 cases. Lymph nodes involved were situated in the axillary area in 3 cases, and in the iliac, deep cervical, supraclavicular, and parotid areas in one case each. Three patients had been given antibiotics without effect; 6 were ill with fever or pain. Treatment in 6 cases was by excision of the affected lymph nodes, which were suppurating in 2 cases. At the time of operation lymphadenopathy had lasted for 10 to 33 days. The wounds healed rapidly and the patients were well within a few days. Histological findings were typical of the disease; bacteriological examination was negative. The 7th patient presented with a right parotid mass, which was subsiding after 7 weeks. It drained spontaneously 2 months later, and healed after a further 4 months. The authors consider that illness and incapacity were curtailed by operation, and suggest that it may be the treatment of choice when the diagnosis is clear, the disease prolonged and severe, and the lesions are suitably placed. *G. C. R. Morris*

985. **Varicella Pneumonia in Adults**
R. H. FITZ and G. MEIKLEJOHN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 489–499, Nov., 1956. 6 figs., 16 refs.

Varicella pneumonia has rarely been diagnosed. However, since radiography of the chest is seldom applied to patients with an acute chicken-pox rash, the condition may be rather more common than is supposed; and, as pointed out in this paper from the University of Colorado, it can be subclinical. The typical clinical picture of a virus pneumonia appearing within a few days of the onset of a chicken-pox rash has been reported in only 15 cases in the United States since the initial case in 1942 (*Arch. intern. Med.*, 1942, **69**, 384), and in one case from Australia; 4 of these 16 patients died.

The present paper deals with no fewer than 12 cases seen in Denver, Colorado, within a period of 5 years (6 of them within 6 months). The age range of the 12 patients was 25 to 42 years, with one exception (61 years); this was strikingly similar to that of the 16 cases previously reported—20 to 46 years, with one exception (71 years). The wide variation in the extent and clinical severity of this form of pneumonia is clearly shown. The cases are divided into 4 groups. In Group I (3 cases) the pneumonia was massive, fulminant, and rapidly fatal; in Group II (5 cases) it was extensive and severe, making the patient's condition critical for a few days; in Group III (3 cases) it was moderately severe, with both clinical and radiographic signs of pneumonia less extensive than in Groups I and II; and in Group IV (one case) it was subclinical, the condition having been diagnosed by a chest radiograph taken at the right time. In all cases the signs of pneumonia appeared within one to 4 days of the onset of the rash, cyanosis being a feature of the more severe cases. The chest radiograph showed nodular, patchy, and miliary bilateral infiltrations of varying extent, usually filling most of the lung fields in Groups I and II. The blood picture was mostly typical of generalized virus infection. Signs of myocarditis were commonly revealed by the electrocardiogram. At necropsy in the 3 fatal cases a widespread, necrotizing, haemorrhagic pneumonitis characteristic of virus pneumonia was found. Type-A nuclear inclusion bodies were demonstrated in various tissues in all 3 cases.

No substantial evidence was obtained that chemotherapy had a specific effect on the illness; in one desperately ill case in which cortisone was given along with antibodies, the role which it played in the recovery of the patient could only be a matter for speculation.

[This paper must take pride of place among the various accounts in the literature of this complication.]

H. Stanley Banks

986. **Acute Infections of the Respiratory Tract and the Adenoviruses**
D. A. J. TYRRELL, D. BALDUCCI, and T. E. ZAIMAN. *Lancet* [*Lancet*] **2**, 1326–1330, Dec. 29, 1956. 2 figs., 22 refs.

Of 7 epidemics of acute respiratory disease (4 among soldiers and 3 among school-children), which occurred in northern England between 1952 and 1955, 6 were studied with special reference to evidence of infection with the adenoviruses. In all cases complement-fixation tests for influenza A, B, and C, and adenovirus antibodies were carried out. In addition, isolation of adenovirus from throat and nose swabs was attempted in cultures of human epithelial cells.

The clinical features of adenovirus infection resembled those of influenza, but in one epidemic the disease was milder, with less pyrexia and less obvious constitutional symptoms and nasal obstruction or discharge. A sore, inflamed throat and hoarse voice were commoner in adenovirus than in influenza-virus infection. In one epidemic in a residential boys' school gastro-intestinal symptoms and conjunctivitis were common. Of 303 paired specimens of sera tested, 42 were positive for adenovirus infection. In a few cases adenoviruses of Type 3 or Type 7 were isolated; in one instance the virus which was isolated was different from all known adenovirus strains.

The authors emphasize that in many cases of epidemic and sporadic respiratory disease clinically resembling those due to adenoviruses there is no evidence of infection with these or other agents. *D. Geraint James*

987. **Treatment of Chronic Enteric Carriers with Penicillin and Probenecid**

C. G. NICOL. *Medical Officer* [*Med. Offr*] **96**, 391–392, Dec. 28, 1956. 2 refs.

During 1954 the author, on behalf of the Ministry of Health, London, visited a large number of mental hospitals at 15 of which 57 chronic typhoid and 13 paratyphoid carriers had been treated with an intensive course of penicillin and probenecid according to the regimen recommended by Rumball and Moore (*Brit. med. J.*, 1949, **1**, 615), namely, 2,000,000 units of procaine penicillin given 3-hourly and probenecid, 0·5 g. 6-hourly for 7 days, or alternatively according to that of Parker *et al.* (*J. clin. Invest.*, 1953, **6**, 593) consisting in 3,000,000 units of crystalline penicillin 6-hourly and probenecid, 1·5 g. three times daily for 10 days; the aim of both regimens is to achieve and maintain a bactericidal level of penicillin in the blood.

The results were disappointing. Only 2 hospitals were wholly cleared of infection, and only 18 typhoid (31·6%) and 5 paratyphoid (37·9%) carriers have remained negative in regard to excretion of *Salmonella typhosa* or *S. paratyphi* since treatment; the longest period of observation was 2 years. In 10 cases there were serious side-effects or complications [not detailed] and one patient aged 76 years died of coronary occlusion shortly after treatment had been completed.

The author concludes that the treatment is not suitable for the type of semi-bedridden carrier found in a mental hospital and that the best hope lies in continuing to exercise scrupulous care in the management and nursing of such carriers, who in general have little capacity to respond to hygienic training. *I. M. Librach*

988. **Calcium Metabolism and Bone Changes in Sarcoidosis**

G. MATHER. *British Medical Journal* [*Brit. med. J.*] **1**, 248–253, Feb. 2, 1957. 4 figs., 34 refs.

Radiographs of the hands and feet of 120 patients at King's College Hospital, London, with sarcoidosis (histologically proved in 80) revealed bone changes in 9, a coarse reticular pattern being seen in 2, cysts in 2, and intermediate states of medullary and cortical bone replacement in 5. Hypercalcaemia was noted in 4 out of 86 patients in whom the serum calcium level was determined, but no correlation was observed between this level and the bone changes. There were no demonstrable bone changes in the 4 patients with hypercalcaemia, and the serum level was normal in 6 of the 9 patients with bone changes. In one case calcium balance studies showed that calciferol caused hypercalcaemia and hypercalciuria, with a corresponding fall in the faecal excretion of calcium; this disturbance of calcium metabolism was corrected by administration of cortisone. In another case, in which calciferol had been discontinued 3 months previously, it was found that cortisone lowered the serum calcium level to normal. The author emphasizes the danger of calciferol therapy, and draws attention to another [well recognized] fact—namely, the relationship between cutaneous and bone sarcoidosis; 5 of the 9 patients with bone lesions had cutaneous sarcoidosis.

[Unfortunately, these time-consuming, if interesting, studies do not draw attention to the occurrence or frequency of hypercalciuria in the presence of a normal serum calcium level. The author's conclusion that routine determination of the serum calcium level is unnecessary is as questionable as his statement that bone lesions seldom cause symptoms or demand treatment.]
D. Geraint James

989. **Infectious Reticulo-Endotheliosis**

L. F. KOYL. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **75**, 709–714, Nov. 1, 1956. 1 fig., 2 refs.

The author reports a series of 205 cases of a condition related to glandular fever occurring in private and consultant practice in Toronto. Of his patients, 9 were children under 12 years of age, 136 were adult females, and 60 adult males. The chief clinical features were weakness, irritability, anorexia, nausea, a non-productive cough, colicky abdominal pain, and, in women, irregular menstruation. Drenching night sweats and lightheadedness associated with bradycardia, hypotension, and jaundice were noted in a few cases.

The clinical finding most characteristic of the disease was moderate enlargement of the lymph nodes which, on palpation, were firm, freely movable, and only slightly tender; 193 patients had enlarged nodes in the neck, 112 in the axillae, and 122 in the groin. In the majority of cases (188) there was considerable swelling and oedema of the lymphoid tissue of the posterior nasopharynx, and in 3 cases there was ulceration of the hypertrophied follicles. Splenomegaly was observed in 82 cases and the liver was palpable in 40. Bowel symptoms were sufficiently severe in 15 patients to warrant sigmoidoscopy. In most cases there was only patchy erythema of the mucosa, but in 3 cases small, shallow ulcers could be seen.

The principal laboratory findings were haematological. In the first week there was often leucopenia; later there was frequently a lymphocytosis. In 50 cases the circulating mononuclear cells outnumbered the neutrophil granulocytes on one or more occasions. The characteristic cell was a monocyte, often twice as large as normal, which frequently showed cytoplasmic and nuclear vacuolation and a distorted nucleus. Later in the disease an abnormal lymphocyte became the predominant cell. The Paul–Bunnell test was negative in the 3 cases in which it was performed. Of 122 patients tested, all had urobilinuria.

The duration of the disease ranged from 4½ to 14 months. Treatment was symptomatic, but in a few cases cortisone appeared to induce a remission. The incubation period seemed to be about 6 weeks. The author considers that all the clinically related glandular fevers should be grouped together irrespective of the Paul–Bunnell reaction. *B. Ruebner*

Tuberculosis

990. **The Efficacy of BCG-vaccination. Epidemic of Tuberculosis in a State School, with an Observation Period of 12 Years.** [In English]
T. V. HYGE. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] **32**, 89–107, 1956. 2 figs., bibliography.

The author reports the results of a 12-year follow-up study of the 368 girls who were attending a Danish state school in which an epidemic of tuberculosis occurred early in 1943, as previously described (*Ugeskr. Læg.*, 1946, **108**, 1151; *Abstracts of World Medicine*, 1947, **1**, 438). The girls had been tuberculin tested during the previous December (1942) and at that time 105 were found to be tuberculin-negative, 133 tuberculin-positive as a result of B.C.G. vaccination, and 130 tuberculin-positive from a previous natural infection.

Of 94 tuberculin-negative pupils exposed to the infection (which was traced to one of the teachers), 70 became tuberculin-positive, 41 developed demonstrable primary pulmonary lesions, 10 primary pleurisy, one primary tuberculous pericarditis followed by post-primary pulmonary tuberculosis, and one peritonitis. During the 12-year follow up 14 cases of post-primary pulmonary tuberculosis developed, 8 of these showing evidence of cavitation. There was one death.

In contrast, of 106 B.C.G.-vaccinated girls (of whom 3 had been re-vaccinated) exposed to the same source case under the same conditions as the tuberculin-negative girls, only 2 developed progressive pulmonary tuberculosis during the 12-year period. On the basis of the findings in the tuberculin-negative group 46 cases of primary and 15 cases of post-primary disease might have been expected if no vaccination had been given. Of the 105 tuberculin-positive pupils exposed to infection, 9 developed progressive pulmonary tuberculosis in the ensuing 12 years.

The author concludes that it is evident from these findings that in the circumstances of the investigation B.C.G. vaccination conferred substantial protection against both primary and post-primary tuberculosis.

T. M. Pollock

991. **Correlation of Tomographic and Bronchographic Findings in Apical Bronchiectasis**
J. H. JUHL, W. L. ALT, and R. H. WASSERBURGER. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **74**, 388–399, Sept., 1956. 7 figs., 18 refs.

The presence of bronchiectasis in chronic tuberculous lesions of the apex of the lung may have an important bearing on treatment, especially if resection is being considered. For this reason the authors have attempted to evaluate the use of tomograms as an additional aid to the bronchogram in the radiological investigation of such cases. At the Veterans Administration Hospital, Madison, Wisconsin, they have studied the radiographs of 100 tuberculous patients in whom satisfactory bronchograms with iodized oil had been made and who had also been examined by tomography. The finding as to the presence or absence of bronchiectasis was recorded in each case by the three authors working together.

The patients were divided into four clinical groups, namely, those with (1) minimal tuberculosis, (2) moderately advanced disease, (3) far advanced disease, and (4) those who had undergone thoracoplasty or plombage. The tabulated results show that of the 18 patients in Group 1, 11 showed no bronchiectasis by either technique and 2 minimal bronchiectasis by both methods. There was "over-reading" of the degree of bronchiectasis in the tomograms as compared with the bronchograms in 4 cases and "under-reading" in one. Of 53 cases in Group 2 there was no evidence of bronchiectasis in 5, and minimal to moderate bronchiectasis (so diagnosed by both methods of examination) in 25. In 7 the tomograms were over-read and in 16 under-read. Of the 24 cases in Group 3 bronchiectasis was detected by both methods in 22, being of comparable degree in 20; the tomograms were over-read in one case and under-read in 2. Of the 5 patients with long-standing thoracoplasty in Group 4, 3 showed comparable bronchiectasis by both methods of examination. In one case the tomogram was over-read and in one under-read.

The results showed that there was a tendency to over-read the tomograms in minimal disease and to under-read them in advanced disease. There was, however, sufficiently good correlation to justify the conclusion that tomography is a useful adjuvant to bronchography and, in cases in which the latter is contraindicated, possibly an alternative to it.

A. M. Rackow

992. **Basal Plombage**
J. K. CLAREBROUGH and W. P. CLELAND. *Thorax* [*Thorax*] **11**, 201–208, Sept., 1956. 12 figs., 6 refs.

Basal plombage has been used by the authors at the Brompton Hospital, London, in the treatment of persistent tuberculous cavities in the lower lobes of the lungs in 9 cases in which simpler measures had failed and in which resection or thoracoplasty were considered impracticable. The procedure employed was a modification of the operation of "thoracolysis" described by O'Shaughnessy and Mason (*Brit. med. J.*, 1939, **1**, 97). Since the aim of the operation is to mobilize the cavity as widely as possible and to maintain the lung in the relaxed position the mobilized area extends to two ribs above and two ribs below the cavity, and for a similar distance horizontally. The periosteum is stripped from the deep aspect only of the selected ribs, and the intercostal muscles are divided posteriorly but are left attached to the lung together with the deep layer of periosteum. The lung is mobilized from the costo-vertebral gutter and the sides of the vertebrae, and the divided muscles

are sutured to the anterior longitudinal ligament of the spine so that all the exposed parietal pleura is covered with a layer of muscle. The space between the lung and the ribs is then filled loosely with either hollow plastic spheres or solid plastic balls and drained for 24 to 48 hours.

The operation has been performed so far on 9 patients with cavities in the apex of the lower lobe. Of these, 2 in whom the procedure was apparently successful died, one suddenly 12 months after operation from cardiac failure and the other 2 years postoperatively from uraemia. The 7 survivors, however, have been followed up for periods ranging from 2 to 7 years; all are well, sputum-negative, and show no radiological evidence of cavitation, and 6 of them are working full-time. The extent of the disease in other parts of the lung and the poor respiratory reserve were the factors contraindicating resection or thoracoplasty. The operation was found to have remarkably little effect on respiratory reserve, and only one patient was made more breathless by the operation.

The authors conclude that basal plombage has a place in the treatment of lower-lobe cavitation when other methods have failed or are inapplicable, and describe their experience in the present small series as " extremely encouraging ". *F. J. Sambrook Gowar*

993. **The Gastric Condition in Pulmonary Tuberculosis. Changes during Treatment with Antituberculous Drugs.** (L'état gastrique des tuberculeux pulmonaires. Ses modifications au cours du traitement par les antibiotiques)
J. CHENEBAULT and P. BERTIN. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 3497–3505, Nov. 14, 1956. 4 refs.

This report is based upon observations of the condition of the stomach in 115 patients with pulmonary tuberculosis at the Hôpital Colombain, Casablanca, all patients with a history of alcoholism, peptic ulcer, or gastric tuberculosis being excluded. The patients were given 0·5 mg. of histamine intramuscularly and the gastric secretions aspirated continuously, the free and total acidity therein being estimated, using Töpfer's reagent as an indicator, and graphs constructed from the results. The shape of these curves, the maximum acidity, the total volume of the secretion, and the appearance of the gastric juice were adopted as criteria of the presence of gastritis.

In 108 of the patients there was some evidence of gastritis, this being moderate or severe in 51%. There was, however, no relation between gastric symptoms (usually slight or absent) and the severity of the gastritis. The condition seemed to progress through increasing hypochlorhydria to achlorhydria, and less frequently to hyposecretion. The condition was more severe in older male patients suffering from malnutrition. The extent of the gastritis was also related to the severity and duration of the tuberculosis, and the gastric condition improved quite rapidly and effectively in the course of treatment of the pulmonary disease with streptomycin, isoniazid, and PAS by infusion. The authors believe that this chemotherapy has a direct effect upon the condition of the gastric mucosa. *I. Ansell*

994. **The Surgical Treatment of Pulmonary Tuberculosis in Childhood and Adolescence**
D. W. HUISH. *Thorax* [*Thorax*] **11**, 186–200, Sept., 1956. 11 figs., 46 refs.

Twenty-nine cases of pulmonary tuberculosis in children under the age of 16 years treated by major surgical procedures have been reviewed. Fifteen cases were operated upon for primary lesions, 14 for chronic " adult type " lesions. The literature relating to the pathogenesis and surgical pathology of pulmonary tuberculosis in children has been reviewed, and an attempt has been made to define the indications for operation on a pathological basis.

It is concluded that surgery has a place in the treatment of primary pulmonary tuberculosis in childhood. Up to the present it has been employed mainly for the removal of irretrievably damaged lung tissue, but with the aid of more accurate pathological diagnosis there is a prospect of employing surgery to prevent such damage. The indications for surgical treatment of chronic pulmonary tuberculosis in children and adolescents are much the same as in adults, but collapse operations have little place and in this age group resection is the method of choice.—[Author's summary.]

EXTRA-RESPIRATORY TUBERCULOSIS

995. **The Treatment of Renal Tuberculosis with Reference to 550 Cases Observed in Hospital during a Period of Ten Years.** (Réflexions sur le traitement de la tuberculose rénale. A propos de 550 cas observés en 10 ans en milieu hospitalier)
J. R. DEBRAY and P. DREYFUS. *Presse médicale* [*Presse méd.*] **64**, 1637–1639, Oct. 10, 1956. 3 refs.

The authors present the result of their observations of 550 cases of renal tuberculosis seen between 1946 and 1956 at the Saint Louis (1946–52) and Lariboisière (1952–6) Hospitals, Paris. They note the changes in the surgical and medical outlook which have taken place since the advent of antibiotics, and describe their present line of treatment.

Four types of renal tuberculous disease are distinguished and discussed. (1) Lesions which are irreversible without surgical treatment; these should be recognized as such at the outset by careful urography, and may require total or partial nephrectomy for unilateral parenchymatous disease and also the surgical treatment of ureteral stenosis or of small contracted bladder. In cases of bilateral disease one kidney with an extensive focus of disease may be removed with confidence provided the lesion in the other kidney is small and antibiotics are given to provide protection for the excretory tract and control of the disease. In recent years antibiotics have made nephrectomy possible in cases previously unsuitable for this operation, but this has been offset by the increased number amenable to medical treatment, so that although 70% of cases of renal tuberculosis in the period 1946–50 were treated by nephrectomy, between 1950 and 1955 this figure fell to 57%. The authors found that after nephrectomy for

unilateral disease the other kidney was rarely attacked; in the case of bilateral lesions ureteral and vesical sequelae occurred in patients who failed to attend for the necessary postoperative supervision, consisting in antibiotic treatment and frequent urographic examinations.

(2) The second type is represented by lesions suitable for medical treatment, such as tuberculous bacilluria alone or cases showing small single or bilateral renal tuberculous foci. (3) Intermediate cases of greater extent than those of Type 2, in which a trial period of antibiotic treatment for 2 to 6 months may show either regression or otherwise and so clarify the decision for or against surgical treatment. Of 180 such cases seen in the last 5 years, total nephrectomy was performed in 152 and partial nephrectomy (reserved for limited polar lesions only) in 28. (4) Irreversible lesions unsuitable for surgery, manifested by extensive bilateral disease or extensive disease of a sole remaining kidney. However, even in this precarious state prolonged and systematic antibiotic treatment has resulted in improved general health in these patients, with prolongation of life, and the possibility of a nearly normal existence. In medical treatment the authors employ for the first few weeks a combination of streptomycin (1 g. daily intramuscularly), with isoniazid (0·15 to 0·3 [presumably grammes, although the unit is not stated] intravenously) and PAS by perfusion, followed by isoniazid and PAS, and if treatment is long continued, PAS by mouth. Courses of treatment may last for 6, 9, 12, or even 18 months. The problem of management after cessation of treatment is briefly discussed. At the present time it is the authors' custom to give a yearly prophylactic course of chemotherapy of 2 or 3 months' duration.

[The survival rate among these patients is not discussed.] *V. Reade*

996. **Tuberculous Meningitis: Combined Corticosteroid and Antimicrobial Therapy**

S. J. Shane, S. E. Copp, and T. K. Krzyski. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **75**, 631–634, Oct. 15, 1956. 18 refs.

The results obtained with corticosteroids in conjunction with antimicrobial agents in the treatment of tuberculous meningitis are reported from Edward Point Hospital, Sydney, Nova Scotia. Reasons why antimicrobial therapy alone is considered inadequate are presented and discussed. The 27 patients included in the trial all received streptomycin, PAS, and cortisone, and a number of them isoniazid as well. Of these patients, 25 are alive and well, 2 having died while under treatment. There was no evidence of exacerbation of non-meningeal tuberculosis or of the occurrence of significant intercurrent non-tuberculous infections resulting from the use of cortisone. Results in 5 cases previously treated without corticosteroids are tabulated to show the marked improvement which followed the addition of cortisone to the treatment.

The authors consider their series too small for statistical treatment, and point out that the study was of necessity carried out without controls. To support their own impressions of the advantages of the "corticosteroid–antimicrobial regimen" they draw attention to the good results obtained with this treatment by Ashby and Grant (*Lancet*, 1955, **1**, 65; *Abstracts of World Medicine*, 1955, **18**, 19). They conclude: "It would appear . . . that there are certain advantages to the use of corticosteroids in combination with antimicrobial agents in tuberculous meningitis, even when the antimicrobial therapy includes isoniazid; and that these advantages are more subtle than the recovery figures, considered alone, would indicate". *John Taubman*

997. **The Treatment of Optic Neuritis and Optic Atrophy in Tuberculous Meningitis.** (Лечение некрита и атрофии зрительного нерва при туберкулезном менингите)

B. A. Tokareva. *Проблемы Туберкулеза* [*Probl. Tuberk.*] 37–41, No. 5, Sept.–Oct., 1956.

The author reports the results of a complex treatment given to 20 children aged one to 12 years who were suffering from optic neuritis or optic atrophy as a result of tuberculous meningitis. The treatment included dilatation of the optic vessels with atropine and the retrobulbar injection of strychnine, the administration of stimulants, aloes, conserved blood, and placental tissue, together with streptomycin and PAS given by ionophoresis to the eyes, after the method of Bourguignon, in doses according to age. This treatment, combined with the administration of streptomycin, PAS, and "phthivazide" [? isoniazid] in the usual way, resulted in improvement in 11 patients (55%).

It is stressed that the treatment must be started very early, that is, as soon as the first signs of change appear in the optic nerves. *H. W. Swann*

998. **The Treatment of Tuberculous Meningitis in the Isoniazid Era.** (Die Behandlung der Meningitis tuberculosa in der Isoniazid-Ära)

E. Rossi and B. Cappis. *Helvetica paediatrica acta* [*Helv. paediat. Acta*] **11**, 346–375, Oct., 1956. 8 figs., bibliography.

The results of treatment of 39 unselected cases of tuberculous meningitis seen at the Children's Hospital, Zürich, between September, 1952, and January, 1956, are reported. Of the 38 patients followed up for a minimum of 6 months after the start of treatment [which the authors consider sufficient time for the evaluation of the results] 9 died, including 5 (out of 11) under the age of 2 years; 2 of the survivors are decerebrate idiots.

The drugs given in treatment were isoniazid, streptomycin, PAS, and cortisone [in no fewer than 10 different combinations without any apparent plan]; in some instances isoniazid, streptomycin, or hydrocortisone was administered intrathecally. Intercurrent staphylococcal meningitis requiring appropriate antibiotic therapy developed during treatment in 4 cases. There were 3 relapses, with one death.

[The authors do not consider that intrathecal administration is now necessary; they used it very little. Their results, however, are poor by current standards.]

John Lorber

Venereal Diseases

999. **The T.P.I. (Nelson) Test in Latent Syphilis.** (TPI-testen (Nelson) ved latent syfilis)
T. MUNKER. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **119**, 79–82, Jan. 17, 1957.

1000. **Some Observations on the TPI Test: Assessment of Results According to the Clinical Data: Influence of Some Variables on Partial Specific Immobilization**
N. HARDY, L. J. BOREL, G. DAGUET, and P. DUREL. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 91–93, June, 1956. 1 fig., 2 refs.

The authors, working at the Hôpital St. Lazare, Paris, have compared the distribution of positive, doubtful, and negative results of the treponemal immobilization test in 469 sera from untreated cases sent for diagnosis with that in 453 samples from patients who had already been treated for syphilis. Of the sera from untreated cases, 15 (3·2%) were found to give a " specific immobilization " (S.I.) of between 20 and 90%, whereas of the sera from treated cases, 93 (21%) gave an S.I. within this range, while a further 198 gave an S.I. of below 20%. These results show a tendency towards negativity as the result of treatment.

The experimental factors affecting partial immobilization were then studied by repeated examination of the same serum. It was found that increasing the incubation period from 17 to 22 hours resulted in a rise in the S.I. from 34 to 56% (mean of 20 observations for each period of incubation). Although in tests carried out in the same conditions appreciable differences in S.I. may be observed, these are not usually sufficiently significant to affect the classification of the serum under consideration. *P. J. L. Sequeira*

1001. **Characteristics of Resistance or Susceptibility of *Treponema pallidum* to Unfavourable Factors**
L. J. BOREL. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 94–95, June, 1956. 2 refs.

The author does not consider that variations in the sensitivity of the treponemal immobilization test are commonly due to sensitization of the treponemes with rabbit antibody or to anticomplementary activity, provided that the technique described by Nelson is strictly followed. In studies carried out at the Hôpital St. Lazare, Paris, the author found that the proportion of surviving *Treponema pallidum* bore the same relation to the concentration of the inhibitory substance, whether this was antibody, penicillin, or sulpharsphenamine. The susceptibility, however, appeared to be dependent on the rate of metabolism of the organism, being increased by the action of cocarboxylase and diminished by chlorpromazine or by a reduction in the temperature of incubation—thus the dose of toxic agent required to provide 50% immobilization was more than 10 times higher at 5° C. than at 35° C. *P. J. L. Sequeira*

1002. ***Treponema pallidum* Immune-adherence and Haemagglutination**
G. L. DAGUET. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 96–97, June, 1956. 1 ref.

The " immune-adherence " phenomenon is concerned with the specific attachment which occurs between erythrocytes and micro-organisms sensitized with antibody and complement. One method of measuring the immune-adherence is by counting the remaining organisms in the supernatant of the reaction mixture, but as Nelson pointed out, this procedure is, for various reasons, subject to error.

The author therefore describes an alternate method of measurement which makes use of the haemagglutination produced by the immune-adherence. After an incubation period of 25 minutes at 37° C. the erythrocytes are allowed to sediment at room temperature or at 37° C. and the reading is made 60 or 90 minutes later. The pattern of the sediment at the bottom of the tube may appear as a small regular disk indicating no agglutination, or show an increasing amount of granular deposit with crenated edges, which is graded + to ++++ according to the size of the deposit. The results of a number of tests are reported; no haemagglutination was observed where there was no complement or no treponemes, although the control test consistently gave positive readings of ++ to ++++. The optimum conditions for the reaction were also examined.

P. J. L. Sequeira

1003. **An Examination of Kahn's Universal Serological Reaction as an Aid to the Diagnosis of Suspected Latent Syphilis**
A. E. WILKINSON. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 98–103, June, 1956. 9 refs.

Kahn's universal serological reaction consists in a series of quantitative tests with standard Kahn antigen on serum diluted with saline of varying strengths. After shaking and the addition of further saline of appropriate strength the test is read immediately, and again after incubation for 4 and 24 hours at 4° to 6° C. According to Kahn, the titre of precipitation increases with the duration of incubation and is greatest at saline strengths of 0 to 0·3% (Zone I) or 1·5 to 2·1% (Zone III). In patients with syphilis, the titre in the 0·6 to 1·2% range (Zone II) is not increased by incubation, while an increase in titre occurs in patients giving a false positive reaction.

The author reports the results obtained with Kahn's reaction in (1) 39 presumed non-syphilitic subjects, (2) 39 patients with symptomatic syphilis, and (3) 112 patients with positive standard serum tests but no clinical evidence of syphilis. Among the patients in Group 1, three patterns of results were found: 24 sera showed no precipitation in Zone II after 24 hours' incubation, 14

sera produced precipitation in Zone II after 24 hours with greater precipitation in Zones I and III, and one serum produced marked precipitation in all zones after 4 hours and of higher titres after 24 hours; these patterns are similar to those described by Kahn. Of the 39 sera from patients in Group 2, 19 gave no rise in titre in Zone II after incubation, while 13 showed a rise of one dilution, 6 of two dilutions, and one of three dilutions. The 112 patients in Group 3 included 54 with positive treponemal immobilization (T.P.I.) test reactions and 58 with negative T.P.I. test results. Of the former, 34 showed no rise in titre in Zone II on incubation, while 17 showed a rise of one dilution, 2 of two dilutions, and one of three dilutions, while of the latter only 8 showed no rise in titre on incubation and 22 a rise of one dilution, 16 of two dilutions, 8 of three dilutions, and one of four dilutions.

It is concluded that while Kahn's universal serological reaction showed a difference in pattern between syphilitic and non-syphilitic sera, the differences were not sufficiently constant to make the reaction reliable in differential diagnosis. *P. J. L. Sequeira*

1004. **Non-specific Serological Reactions for Syphilis in [Habitual] Blood Donors.** (Reazioni sierologiche aspecifiche per la lue in donatori di sangue)
L. PERUCCIO. *Minerva dermatologica* [*Minerva derm. (Torino)*] **31**, 287–291, Oct., 1956. 3 refs.

After discussing various aspects of biologically false positive reactions in serological tests for syphilis the author, writing from the University Dermatological Clinic, Turin, suggests that qualitative and quantitative changes in the serum globulins may be a possible cause, the fundamental change being stimulation of the plasma reticulum producing deviation from the eucolloid state.

He has noted the appearance of rather weak, transitorily positive, serological reactions for syphilis in one or two out of a large number of tests performed on regular blood donors after repeated donations, these reactions usually appearing shortly after a donation. The tests used were the Wassermann reaction, with either syphilitic liver and beef heart or Sclavo treponin and cardiolipin as antigen, and also the Kahn and microgen flocculation tests. Out of a total of 2,997 donors tested, positive reactions were obtained in 18. Two complement-deviation tests and two flocculation reactions were doubtful, in 6 cases one or two of the flocculation reactions were positive, and in the remaining cases both complement-deviation tests and one or both of the flocculation tests gave positive results. If all doubtful and delayed reactions are discarded the incidence is estimated to be about 4 per 1,000.

All these donors had given a large number of donations over several years and the positive reactions were obtained 2 days to 17 months after the last donation; most of them occurred within 5 to 20 days and subsequently became spontaneously negative. In some cases this transitory reaction recurred in the same patient after a further donation. The author suggests that during the very active production of plasma protein which follows blood donation the hyperactive plasma reticulum of the bone marrow [*sic*] allows incompletely differentiated globulin to escape into the circulation and that this is the cause of the positive reaction. No doubt individual factors play a role and account for the recurrences of such reactions in the same donor, or on the other hand for the over-all rarity of the reactions.

F. Hillman

1005. **The Antibody Titre in Syphilitics Treated with Cortisone.** (Studio del titolo degli anticorpi in luetici trattati con cortisone)
C. ROSSETTI and G. MARSON. *Minerva dermatologica* [*Minerva derm. (Torino)*] **31**, 292–294, Oct., 1956. 26 refs.

The authors first briefly review the conflicting literature on the subject of the antibody titre in syphilitic patients treated with cortisone. They then present, from the University Dermatological Clinic, Padua, the results of the quantitative treponemal immobilization (T.P.I.) test, complement-deviation tests with cardiolipin and treponemal antigens, and the V.D.R.L. flocculation test carried out on 15 patients who had received 200 mg. of cortisone by mouth daily for 10 days. The tests were carried out before treatment and again 5 and 10 days after it. In 3 of the cases regular specific treatment had been given for the preceding 2 years, 5 had received irregular treatment, and the remainder were previously untreated.

On the whole there were no significant changes in the results of the T.P.I. and complement-deviation tests, a few cases only showing a slight, non-significant fall in the titre. There was, however, a distinct, albeit slight and irregular, reduction in the titre of the flocculation reactions. In discussion it is suggested that this may have been due to the greater sensitivity of the flocculation reaction or to a change in the serum induced by cortisone, or to the presence of different, that is deviating and flocculating, antibodies. *F. Hillman*

1006. **Penicillin and General Paralysis of the Insane** (Penicilina e demência paralítica)
A. B. FORTES. *Hospital* [*Hospital (Rio de J.)*] **50**, 645–673, Nov., 1956. 5 figs., bibliography.

In a brief review of the place of penicillin in the treatment of general paralysis of the insane the author stresses the value of high dosage to achieve the requisite " neurological level ". At the Neurosyphilis Hospital, Rio de Janeiro, 30 such patients received intramuscular injections, each of 2·4 mega units of benzathine benzylpenicillin, on the first, fifth, and ninth days of treatment, together with 500,000 units of potassium benzylpenicillin every 12 hours to a total of 20 injections. A second group of 28 patients received daily injections of 1,000,000 units of procaine benzylpenicillin for 10 days. In the first group 25 (83%) of the 30 patients showed clinical improvement after treatment, 4 no change, and one died; in the second group 14 were improved, 13 remained stationary [and the fate of one is not divulged]. In an earlier group treated with malaria and penicillin one-half were improved, one-sixth unchanged, and one-third were worse. *Eric Dunlop*

Nutrition and Metabolism

1007. **Modification of Abnormal Serum Lipid Patterns in Atherosclerosis by Administration of Sitosterol**
M. M. BEST and C. H. DUNCAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **45**, 614–622, Oct., 1956. 6 figs., 8 refs.

Sitosterol is a plant sterol with a chemical structure nearly identical with that of cholesterol, only one ethyl group being added to the side-chain. It has been shown greatly to reduce the absorption of cholesterol from the intestine, either by competition for esterification, or by forming a mixed crystal compound with cholesterol, which is much less soluble than either of the sterols alone.

In an investigation of the effect of sitosterol on the serum lipid level carried out at University of Louisville School of Medicine, Kentucky, 6 to 8 g. of sitosterol was administered to 24 patients three times a day before the main meals for various periods up to 29 months, during which the patients ate a normal unrestricted diet. The mean reduction in the serum cholesterol level was 15·5%, in the serum phospholipid content 9·4%, and in the total lipid content 13·8%. No significant toxic side-effects were detected during the time of the experiment. While the number of patients was too small to permit of any definite conclusion, it appears that on essential hyperlipaemia [for which, incidentally, dietetic treatment is effective] sitosterol exerts only a very modest influence. Of the 11 patients in the series who had suffered myocardial infarction, one had a fatal recurrence after 3 months of sitosterol administration. The remaining 10 have been treated up to 29 months (mean 15·8 months) without any recurrent infarction.

[Although there is good evidence that sitosterol reduces the incidence of cholesterol-induced atherosclerosis in experimental animals, especially chicks and rabbits, the findings presented in this paper do not warrant any conclusion being drawn regarding its effect on human atherosclerosis.] *Z. A. Leitner*

1008. **Physical Activity and the Diet in Populations Differing in Serum Cholesterol**
A. KEYS, J. T. ANDERSON, M. ARESU, G. BIÖRCK, J. F. BROCK, B. BRONTE-STEWART, F. FIDANZA, M. H. KEYS, H. MALMROS, A. POPPI, T. POSTELI, B. SWAHN, and A. DEL VECCHIO. *Journal of Clinical Investigation* [*J. clin. Invest.*] 35, 1173–1181, Oct., 1956. 1 fig., 35 refs.

This paper from the University of Minnesota integrates and summarizes the results of numerous previous studies carried out by Keys and colleagues, and in particular analyses in detail the results obtained in Minneapolis, Malmö (Sweden), Cape Town, Bologna, Sardinia, and Naples. These demonstrated clearly that the serum cholesterol level seems to be related to the proportion of fat-derived calories to the total calories in the habitual diet of the various populations studied. These observations were confirmed by several other groups of workers, but Mann *et al.* (*Brit. med. J.*, 1955, **2**, 1008; *Abstracts of World Medicine*, 1956, **19**, 362) raised the question whether differences in the physical activity of the population groups might not account for these findings. It is pointed out by the present authors that in their global survey not only different racial groups were investigated (as in Cape Town), but within the same population groups the results were compared between men performing light, moderate, and heavy physical work. It was found that the blood cholesterol level was indeed lower in men doing heavy work, and not only in Bantu heavy workers, but also in similar workers in both Malmö and Sardinia. When, however, the diets of these men were scrutinized very carefully, it was found that either the daily fat intake was lower, as was the case in the Bantu heavy worker or, as occurred in Malmö and Sardinia, the men performing heavy physical work increased their total caloric intake substantially by adding carbohydrates to their diet while their fat intake remained about the same as in men doing light and moderate physical work, so that it was in fact relatively lower.

Although in this paper attention is mainly directed to variations in the total serum cholesterol content, reference is also made to similar differences in the cholesterol fraction carried by β lipoproteins. Furthermore, differences in the relative obesity and body weight could not account for the differences in the serum cholesterol level either. It is therefore concluded that the ratio of fat-derived calories to total calories in a subject's habitual diet has greater influence on the serum cholesterol and β-lipoprotein levels than has physical activity *per se*.
Z. A. Leitner

1009. **" Essential " Fatty Acids, Degree of Unsaturation, and Effect of Corn (Maize) Oil on the Serum-cholesterol Level in Man**
A. KEYS, J. T. ANDERSON, and F. GRANDE. *Lancet* [*Lancet*] **1**, 66–68, Jan. 12, 1957. 18 refs.

Although the serum cholesterol level in man appears to be independent of the intake of cholesterol, it can be lowered considerably by replacing the common meat and dairy fats in the diet with carbohydrate and protein. Certain vegetable and fish oils are also said to lower the serum cholesterol level, and this property has been ascribed either to their degree of unsaturation or to their content of " essential " fatty acids.

The effect of three different oils with different unsaturated fatty acid and linoleic acid contents, namely, corn [maize] oil, sunflower-seed oil, and sardine oil, was therefore compared with that of butter fat in studies carried out at the University of Minnesota, Minneapolis, on 26 physically healthy schizophrenic patients who were divided into four groups matched as to age, relative obesity, and physical activity. Before the experiment the subjects were maintained in caloric balance on a fixed diet for several months, including a stabilizing

period of 4 weeks with 100 g. of butter daily. During the experiment the test oils were given in quantities of 100 g. daily, the diet being constant in all other respects and containing about 100 g. of protein, 300 mg. of cholesterol, and 40 g. of mixed fats in addition to the test oils. The fats represented 39·8% of the total caloric intake; caloric balance was maintained with additional carbohydrate if necessary and the diet supplied between 2,900 and 3,400 Cal. daily. The mean body weight remained practically constant during the whole experiment. Two of the groups received corn and sunflower oil respectively and the other two corn and sardine oil respectively for two periods of 14 days, and all four groups butter fat for a third period of 14 days. The total serum cholesterol content and also the cholesterol carried by the alpha- and beta-lipoprotein fractions were determined at weekly intervals.

The mean serum cholesterol level during the daily ingestion of 100 g. of butter was 52 mg. per 100 ml. higher than while taking corn oil, 35·8 mg. per 100 ml. higher than while taking sunflower-seed oil, and 39·8 mg. per 100 ml. higher than while taking sardine oil. At the change-over from corn oil to sunflower-seed oil the total serum cholesterol level rose, and at the change in the reverse direction it fell, the average difference being 9·3 mg. per 100 ml. A similar rise and fall in the total serum cholesterol level was observed on changing over from corn oil to sardine oil and vice versa, the average difference here being 20·2 mg. per 100 ml.; these differences were due in both cases mainly to the changes in the beta-lipoprotein fraction. The authors conclude that " these findings do not support the view that the serum-cholesterol level in man is a simple inverse function of the essential fatty-acid content or of the degree of unsaturation of the fatty acids in the diet ".

Z. A. Leitner

1010. **A Practical Method for the Reduction of Plasma Cholesterol in Man**

H. A. SCHROEDER. *Journal of Chronic Diseases* [*J. chron. Dis.*] **4**, 461–468, Nov., 1956. 36 refs.

In a study of the plasma cholesterol level carried out at Washington University School of Medicine, St. Louis, 20 ambulatory patients with atherosclerosis and/or hypertension were given a diet in which the fat content was reduced from the usual 40% of caloric intake to 20% by excluding all dairy products (which contain short-chain saturated fatty acids) and hydrogenated vegetable oils (containing long-chain saturated fatty acids) and reducing as far as practicable the intake of animal meat fat, particularly pork. Fish was allowed *ad libitum*, and an adequate intake of vegetable fat containing linolenic acid was provided by using soya-bean oil or corn oil for cooking and for salad dressings. In addition calcium disodium ethylenediamine tetra-acetate (EDTA), a chelating agent which has been shown to reduce the serum cholesterol level in some cases, was given in a dose of 1 g. daily by mouth, together with 10 mg. of pyridoxine (vitamin B_6); apparently this vitamin acts as a co-enzyme in the desaturation of certain partly unsaturated fatty acids, promoting the metabolism of linoleate to arachidonate and of linolenate to hexanoate, and deficiency of the vitamin has been shown to produce in monkeys subintimal lesions which are characteristic of early atheroma.

The diet described did not in itself lead to any significant reduction in the serum cholesterol level, but when the calcium EDTA and pyridoxine were added the mean serum cholesterol level fell by 29% in the course of 2 months, although after another 2 months it was only 20% lower than the original mean of 258 mg. per 100 ml. There were no adverse symptoms during the period of study, and 5 patients claimed that their attacks of angina occurred considerably less often while receiving the treatment, but no change was noticed by 2 patients with intermittent claudication. It is suggested that this regimen offers a simple, practicable, and not too restrictive diet for ambulatory patients taking most of their meals at home.

Robert de Mowbray

1011. **Hereditary Hypercholesterolaemic Xanthomatosis**

J. C. LEONARD. *Lancet* [*Lancet*] **2**, 1239–1243, Dec. 15, 1956. 3 figs., 26 refs.

The author has investigated 11 families in which hereditary hypercholesterolaemic xanthomatosis was diagnosed, in 10 cases, after one of their number had been investigated for ischaemic heart disease. Of the total of 67 members of these families examined, 35 had one or more manifestations of the disease, which appears to be transmitted as a simple Mendelian dominant, with equal incidence in both sexes. Until the age of 30 years the only abnormality usually found was elevation of the serum cholesterol level, but after that age clinical changes became apparent, such as xanthomata of tendons and skin, ischaemic heart disease, and intermittent claudication. One man aged 70 died of haemorrhage from an aneurysm of the abdominal aorta.

Laboratory investigations revealed a serum cholesterol level of over 350 mg. per 100 ml. in the majority of affected individuals; in the few subjects studied the total serum lipid level was moderately raised while that of neutral fats was normal. In 4 of the subjects the therapeutic effect of the cholesterol isomer sitosterol was investigated; this substance, by impairing cholesterol absorption from the intestine, is said to lower serum cholesterol levels, but with doses of 18 g. a day and a normal diet the serum cholesterol level fell by no more than 20%. The therapeutic value of sitosterol is therefore considered uncertain. The differential diagnosis and the effects of treatment with low-fat diets and heparin are discussed.

Kenneth Gurling

1012. **Penicillamine, A New Oral Therapy for Wilson's Disease**

J. M. WALSHE. *American Journal of Medicine* [*Amer. J. Med.*] **21**, 487–495, Oct., 1956. 7 figs., 26 refs.

The biochemical changes in Wilson's disease (hepatolenticular degeneration) include an increased concentration of copper in the liver and brain, an increased excretion of copper in the urine, and low levels of copper and ceruloplasmin (the copper-binding α globulin) in the plasma. Having observed that patients with liver damage

treated by parenteral administration of penicillin excrete a degradation product, penicillamine or dimethyl cysteine, in the urine, the author had previously made a preliminary trial of oral treatment with penicillamine in Wilson's disease (*Lancet*, 1956, **1**, 25). In this further study the oral administration of 900 mg. of penicillamine hydrochloride, given in 3 doses of 300 mg. before meals, produced in 2 healthy subjects a twentyfold increase (from 30 to over 600 μg.) in the 24-hour excretion of copper in the urine. In 6 patients with Wilson's disease the average resting excretion of copper in the urine during 24 hours was between 200 and 500 μg.; oral administration of 900 mg. of penicillamine produced very large increases, giving values between 1,000 and 5,000 μg., and the increase was continued into the next day. No toxic reactions were observed in any patient in these short-term trials. In 5 of the 6 cases penicillamine was considerably more effective than an intramuscular dose of 200 mg. of 2:3-dimercaptopropanol (BAL). Further trials are needed to determine whether prolonged administration of penicillamine will be free from toxic reactions, and whether clinical improvement will result from the removal of copper.

Joseph Parness

1013. **Familial Primary Systemic Amyloidosis: an Experimental, Genetic and Clinical Study**

J. G. Rukavina, W. D. Block, and A. C. Curtis. *Journal of Investigative Dermatology* [*J. invest. Derm.*] 27, 111–131, Sept., 1956. 7 figs., 17 refs.

Systemic amyloidosis was diagnosed in two cousins, aged 50 and 52 years, referred to the Hospital of the University of Michigan, Ann Arbor, because of an unusual syndrome. The chief symptoms were increasingly defective vision and numbness and pain in the hands and legs. Ophthalmic examination revealed the presence of semi-opalescent, hyaline-like opacities, while neurological investigation suggested a peripheral neuropathy. The diagnosis was confirmed by skin biopsy in one case and at necropsy in the other. Electrophoresis of the serum proteins in both cases revealed the presence of an unusual fraction " migrating between the β and α_2 globulin areas ".

A study of some 66 relatives of these patients showed that in 37 the electrophoretic pattern of the serum was normal, in 15 there was an abnormal peak between the α_2 and β globulins, and in 14 the pattern was characterized by poor resolution in the α_2 region. The serum lipoprotein concentration was determined in 33 of these relatives by ultracentrifugation. Abnormalities in lipoprotein distribution were common, and were highly correlated with the abnormalities detected by serum electrophoresis.

In many of the members of this family there were clinical signs and symptoms suggestive of amyloidosis, these being most marked when the serum protein pattern was abnormal. Thus in 10 of the 15 subjects showing an atypical peak between the α_2 and β globulins, and in 6 of the 14 whose electrophoretic pattern was poorly resolved in the α_2 region, there were clinical signs and symptoms suggestive of the disease. Of the 13 subjects with an abnormal electrophoretic pattern but no clinical manifestations of the disease, 12 were under the age of 21.

These abnormalities were distributed in the family in a manner consistent with the hypothesis that a single disease process was being inherited as a Mendelian dominant character. The earliest sign of the disease is evidently to be found in the abnormal character of certain of the serum globulins. Clinical signs and symptoms may not develop till later in life, and are rather variable. *H. Harris*

1014. **Genetic, Clinical, Biochemical, and Pathological Features of Hypophosphatasia. Based on the Study of a Family**

R. A. McCance, D. V. I. Fairweather, A. M. Barrett, and A. B. Morrison. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 523–537, Oct., 1956. 16 figs., 22 refs.

Since 1948 several isolated reports have appeared of children in whom the bones were of rachitic type and in whom the major, and probably primary, defect was a very low serum phosphatase level. These reports are reviewed in the present paper, and the picture which emerges from them is of a familial disease characterized by hypophosphatasia and very variable clinical intensity. The bones, teeth, and kidneys may all be involved or on the other hand the only apparent abnormality may be the chemical changes in the serum.

This paper from the University of Cambridge describes 2 further cases of the condition in siblings and also the investigation of the patients' family over four generations. The first case was in an infant, seen at the age of 13½ weeks, who had failed to gain weight and at 8 weeks of age had developed obvious deformities of the feet. In hospital she showed little improvement, developed shallow respiration, and died at 14 weeks. The second patient, a brother of the first, was shown by radiography to have bony abnormalities while still in utero. When he was born there was seen to be gross lack of development of the bony cranium, a large haemangioma of the brow, and beading of the ribs; the long bones were soft and easily bent. Weight was maintained but not gained and death eventually occurred at home at the age of 16 weeks after the sudden onset of cyanosis and " grunting " respiration. Laboratory investigations showed that the serum phosphatase level was below one Bodansky unit per 100 ml., and similar low values were found in the father and in the paternal grandfather. No phosphatase inhibitor could be demonstrated in the serum; the serum calcium and phosphorus levels were raised. In the second case an abnormal amount of phosphoethanolamine in the urine was demonstrated. The post-mortem findings in the 2 infants are described; the main feature was a generalized deficiency of calcification with an excess of osteoid tissue and irregular endochondral ossification.

The condition differs from true rickets in its earlier onset, the failure of the patient to gain weight, the low serum phosphatase level, the high serum phosphorus and calcium content, and the failure to improve on administration of vitamin D. *C. L. Cope*

Gastroenterology

1015. **The Diagnostic Significance of Pulsation of Abdominal Aorta.** (Диагностическое значение пульса брюшной аорты)
G. P. KOVTUNOVICH and G. A. IVASHKEVICH. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 40–43, No. 10, Oct., 1956.

Having noticed the absence of pulsation of the abdominal aorta in some of their patients the authors, in an attempt to establish the possible diagnostic significance of this sign, have examined 1,206 healthy individuals of all ages. They found that in 99·3% of these healthy persons pulsation of the aorta could be felt at the level of the umbilicus. Palpation was carried out on a hard couch, gradually increasing pressure being applied with the superimposed hands during expiration. Although it was impeded by the presence of adiposity or a recent large meal, even when the skin and subcutaneous tissues were over 4 cm. in thickness the pulsation could still be felt. In view of the very high percentage of positive findings in healthy people the authors suggest that the absence of pulsation of the abdominal aorta should be considered pathological.

To determine the diagnostic value of this sign aortic palpation was then attempted in 344 cases. Of these 273 were cases of surgical abdominal emergency, 42 of neoplasm of the gastro-intestinal tract, 21 of lymphadenomatosis, and 8 of tuberculous peritonitis and adenitis.

In patients with an acute abdominal condition but without generalized rigidity of the abdominal wall or pronounced meteorism the abdominal aorta pulsation was as readily elicited as in healthy people; thus out of 128 patients with acute appendicitis or cholecystitis the pulsation was felt in 127, as it was also in 34 out of 35 patients with extrauterine pregnancy or torsion of an ovarian cyst, whereas pulsation could be felt in only 6 out of 26 patients with perforated peptic ulcer, in only 12 out of 63 with acute intestinal obstruction, and in only 6 out of 19 with acute pancreatitis. The failure to palpate the abdominal aorta in conditions accompanied by acute peritonitis or meteorism is self-explanatory, and the absence of pulsation in cases of acute pancreatitis can be explained by the swelling of the pancreas and involvement of the adjacent lymph nodes. In patients with neoplastic disease the pulse is undetectable in cases of secondary deposits in the peri-aortic lymph nodes, and also in cases of abdominal lymphadenomatosis; in some of the latter cases the pulse was palpable after deep radiotherapy, but disappeared again on relapse. In half of the cases of abdominal tuberculosis the pulse could not be felt.

The authors conclude that the sign has diagnostic and some prognostic value in certain cases of neoplastic disease involving the abdomen, and also in acute pancreatitis. *A. Koby*

STOMACH AND DUODENUM

1016. **Late Results of Treatment of Peptic Ulceration by Sleep and Procaine.** (Отдаленные результаты лечения язвенной болезни сном и новокаином)
E. I. SAMSON. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 54–55, No. 10, Oct., 1956. 7 refs.

Of 136 patients suffering from peptic ulceration, 55 were treated by sleep therapy and 81 by intravenous infusions of procaine. Apart from dietary restrictions no other medication was given. Most of the patients in both groups had had many relapses of their symptoms in the past. Sleep treatment was given in darkened wards where sleep was induced by means of narcotics and in some cases by hypnosis, the mean duration of sleep being 14 to 16 hours out of the 24 and the mean length of stay in hospital 20 days.

The immediate results of treatment in both groups were very satisfactory, complete "cure" being claimed in 51 out of the 55 given sleep therapy, and in 70 out of the 81 treated with procaine, while there was amelioration of symptoms in the remainder. The improvement was confirmed by the radiological findings. The long-term results, however, were much less encouraging. In the sleep-treated group relapse was observed in 11 cases within 2 to 3 months, in 12 within 3 to 10 months, and in 8 between 1½ and 2 years. Of the procaine-treated patients 6 relapsed in less than 6 months, 12 in 12 months, 6 in 18 months, 7 in 2 years, and 7 within 2½ years. The rest of the patients are well after 2 to 3 years.

The author [rightly] concludes that the remote results of treatment of peptic ulcer with procaine or sleep only are not satisfactory. *A. Koby*

1017. **Peptic Ulceration and ABO Blood Groups**
J. A. BUCKWALTER, E. B. WOHLWEND, D. C. COLTER, R. T. TIDRICK, and L. A. KNOWLER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 1215–1220, Nov. 24, 1956. 1 fig., 14 refs.

Following reports of the finding of an association between blood Group O and peptic ulceration in the United Kingdom, Scandinavia, and elsewhere in Europe, the authors have investigated the possibility of such an association existing among the semi-rural population of Iowa. For this purpose they have studied the hospital records of patients admitted with peptic ulcer to the University Hospitals and five other hospitals in Iowa between 1940 and 1956. Data obtained from blood banks was used to determine the frequency of blood types in the population from which the patients were drawn, the donors to which these related being regarded as controls. The criteria for the diagnosis of ulcer were strict, and were fulfilled by only one in 6 patients with a clinical diagnosis of ulcer. Separate analysis of the

material thus obtained according to whether the diagnosis was confirmed surgically or by other means showed that there was a slightly increased prevalence of Group-O blood amongst the former. The percentage increase of Group-O blood amongst these patients over that found in the control group was of the order of 7%, and applied to gastric as well as duodenal ulcer; the statistical significance of this finding was of a high order. Information with regard to gastric secretory analysis suggests that the incidence of Group O amongst hypersecretors with duodenal ulcer is highest of all.

The paper concludes with a discussion as to whether the association is purely anthropological and indicative of an ulcer-prone heredity, or whether there is some closer link between the possession of Group-O blood and the development of peptic ulcer. *J. Naish*

1018. **An Analysis of 200 Admissions for Massive Upper Gastrointestinal Bleeding**

S. L. ZIMMERMAN, E. F. ENGEL, B. LAPIDUS, E. A. BRADLEY, and H. CLAYTOR. *Annals of Internal Medicine* [*Ann. intern. Med.*] **45**, 653–661, Oct., 1956. 16 refs.

A critical analysis is presented of all cases of massive gastro-intestinal haemorrhage admitted to the Veterans Administration Hospital, Columbia, South Carolina, between 1947 and 1953, including all those in which the erythrocyte count was less than 3,500,000 per c.mm. or the haemoglobin level was less than 10 g. per 100 ml. at the start of treatment. The 200 cases included 123 of duodenal ulcer, 22 of gastric ulcer, 10 of prolapse of the pyloric mucosa, 29 of cirrhosis of the liver, 3 of carcinoma of the stomach, and 13 in which the site of the haemorrhage was undetermined. Except in those cases in which surgery was considered necessary and practicable, medical treatment was given, with particular regard to the prompt feeding of those patients who were not vomiting.

In the group of 123 cases of duodenal ulcer, emergency surgery because of uncontrolled haemorrhage was necessary in only 2. There were 3 deaths in this group, but haemorrhage was the cause of death in only one, a mortality from haemorrhage of 0·8%, which compares very favourably with reported figures. Of the 121 patients treated medically, 46 were re-admitted to hospital for haemorrhage, and of these, 24 were subsequently subjected to surgery following control of the haemorrhage.

In the group of 22 cases of gastric ulcer, one patient underwent gastric resection during the episode of haemorrhage, with recovery. There were 5 deaths in this group, 3 being the result of the gastric haemorrhage, giving a mortality of 13·6%; this figure lends support to those who advocate earlier surgical intervention in cases of bleeding gastric ulcer. Gastric resection was carried out in 4 cases after the haemorrhage had been controlled by medical measures.

[The authors do not state explicitly whether the 200 patients were experiencing a first haemorrhage; there is no mention of a previous haemorrhage, except in one case of prolapsed antral mucosa.]

Joseph Parness

1019. **Acute Hemorrhage from Peptic Ulcer: a Follow-up Study of 310 Patients**

A. B. CHINN, A. S. LITTELL, G. F. BADGER, and A. J. BEAMS. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 973–978, Nov. 22, 1956. 2 figs., 9 refs.

Of 310 patients who had one or more episodes of acute bleeding due to peptic ulcer at University Hospitals [Cleveland, Ohio] between 1936 and 1948, 94·2% were followed until July 1, 1951, for information about subsequent acute hemorrhage, death from subsequent acute hemorrhage or other ulcer complication, and death from causes unrelated to ulcer.

Of the 173 patients whose index hemorrhages were due to duodenal ulcer and who had had no hemorrhages or operations before the index hemorrhage, those patients who survived the index hemorrhage and were continued under medical management had a 31% chance of having a second hemorrhage within 5 years of the first; those who survived a second hemorrhage and were continued under medical management had a 64% chance of having a third hemorrhage within 5 years of the second.

The age of the patient did not influence the chance of having a second hemorrhage from duodenal ulcer, but the mortality from the initial hemorrhage, and probably from subsequent hemorrhages, increased with age. Survival from a massive hemorrhage from duodenal ulcer did not appear to alter the risk of later death from causes other than ulcer. The patient with duodenal ulcer who had had multiple acute hemorrhages and was over 50 years of age offered the least favorable prognosis for continued successful medical management. The mortality from the initial hemorrhage from gastric ulcer was markedly higher in patients over 50 years of age than in younger patients.—[Authors' summary.]

1020. **Continuously Recorded *in situ* *p*H of Gastric and Duodenal Contents in Patients with and without Duodenal Ulcers**

R. A. ROVELSTAD. *Gastroenterology* [*Gastroenterology*] **31**, 530–537, Nov., 1956. 2 figs., 18 refs.

In this paper from the Mayo Clinic are described studies on the *p*H of gastric and duodenal contents in 21 patients with active duodenal ulcer. For comparison the *p*H was also recorded in 23 patients with dyspepsia of psychogenic origin. The recordings were made by means of a shielded glass electrode with a radio-opaque leader which, after fasting for 12 hours, the patient swallowed, the position of the electrode being controlled radiologically. The reference calomel half-cell made contact with a saturated solution of potassium chloride in which the unabraded left index finger was immersed. The *p*H was recorded continuously for about 3 hours by means of a Beckman *p*H-meter with a Brown strip-chart recorder. Control recording was done for at least 30 minutes, after which 0·01 mg. of histamine base per kg. body weight was injected subcutaneously. Duodenal acidity was studied in 14 patients with ulcer and in 10 of the control subjects, gastric acidity in all the subjects. In addition a standard test meal was given and the stomach contents sampled in one hour for free hydrochloric acid, titration being against 0·1 N sodium hydrox-

ide with Töpfer's reagent as indicator. The *p*H readings were analysed in terms of the means of the corresponding values of linear equivalents—namely, mEq. per litre. The significance of differences was estimated by Student's " t " test.

The mean values of *p*H of gastric and duodenal contents obtained are shown in the following table:

	Gastric Fasting *p*H	Duodenal *p*H	
		Fasting	After Histamine Injection
Controls (irritable bowel) ..	2·4	3·9	3·8
Duodenal ulcer ..	1·9	3·6	2·6
Test of significance of difference	P<0·01	P>0·05	P<0·05

A rough correlation was found between the rise in free gastric acidity after a test meal and the fall in duodenal *p*H after histamine stimulation. With the arbitrary level of *p*H 4, the frequency of duodenal readings below this was studied. There was no difference in fasting values as between the ulcer and control patients. After histamine stimulation the ulcer group showed *p*H values below 4 for a significantly longer period than did the controls.

The author discusses the practical implications of this technique, and compares his results with those previously reported by others using aspiration methods.

T. J. Thomson

1021. **Subtotal Gastrectomy with and without Vagotomy for Duodenal and Gastrojejunal Ulcer. Present Status**
R. COLP. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 1599–1603, Dec. 29, 1956. 7 refs.

1022. **Occurrence of Gastric Cancer in Persons with Achlorhydria and with Pernicious Anemia**
J. BERKSON, M. W. COMFORT, and H. R. BUTT. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **31**, 583–596, Oct. 31, 1956. 2 figs., 19 refs.

In this detailed report from the Mayo Clinic are presented the results of a long-term critical survey of the relationship of gastric carcinoma to achlorhydria and pernicious anaemia. The material studied consisted of 1,058 subjects within an age range of 30 to 59 years. Of this total, 837 (403 males; 434 females) had simple achlorhydria and 221 (117 males; 104 females) achlorhydria with pernicious anaemia. When first included in the study none of these patients showed evidence of gastric carcinoma. Of the total of 1,058 subjects, 1,037 (98%) were followed up for 10 years and 1,021 (96·5%) for 15 years.

In the group with simple achlorhydria it was found that over a 15-year period the survival rate for males was 78·8%, the calculated expected rate for the general population being 78·4%; the survival rate for females was 84·6% compared with an expected figure of 85·2%. In the group with pernicious anaemia the survival rate of the females was 84·2%, the calculated survival rate being 82·7%. It was amongst the males of this group, however, that a significantly increased mortality first emerged, the observed 15-year survival rate being 63·5% compared with a calculated rate of 73·5%. These studies were of survival rates as determined for deaths from all causes, and not those due to gastric carcinoma alone, it being pointed out that, although gastric carcinoma has a high fatality, its incidence is relatively small, so that the mortality rate would not have a significant effect on survival rates as a whole.

A direct study of mortality figures for gastric carcinoma was then made on the 207 deaths in the series. In each group the observed number of deaths due to gastric carcinoma greatly exceeded the calculated expected figure. Consideration of the total for the entire series shows that whereas the expected number of deaths due to gastric carcinoma was 4·5, the observed number was 26. For various reasons the authors considered that this ratio for gastric carcinoma in subjects with achlorhydria and pernicious anaemia was too high and may reflect faulty sampling. They do not deny, however, that the incidence of gastric carcinoma is higher in subjects with achlorhydria and/or pernicious anaemia than in the general population. *J. N. Harris-Jones*

LIVER

1023. **Cerebral Metabolism in Hepatic Insufficiency**
J. F. FAZEKAS, H. E. TICKTIN, W. R. EHRMANTRAUT, and R. W. ALMAN. *American Journal of Medicine* [*Amer. J. Med.*] **21**, 843–849, Dec., 1956. 3 figs., 14 refs.

This paper from the District of Columbia General Hospital, Washington, D.C., is concerned with studies of cerebral metabolism in 51 patients with liver disease, 20 of whom were alert, 15 had signs of moderate cerebral dysfunction, and 16 were in hepatic coma. The observations made included electroencephalography and determination of the blood oxygen, ammonia, and pyruvate levels and cerebral blood flow—estimations from which the cerebral uptake of oxygen, ammonia, and pyruvate could be calculated.

Cerebral oxygen consumption was depressed even in the absence of clinical neurological disturbances, and grossly depressed in the patients with coma. Although blood ammonia and pyruvate levels were often increased, the rate of cerebral uptake was normal, and there was no definite correlation between blood ammonia level and neurological status. *D. A. K. Black*

1024. **The Serum Alkaline Phosphatase in Chronic Infiltrative Disease of the Liver**
R. S. ROSS, F. L. IBER, and A. M. HARVEY. *American Journal of Medicine* [*Amer. J. Med.*] **21**, 850–856, Dec., 1956. 1 fig., 32 refs.

The possibility is discussed that in some patients with liver disease an elevation of serum alkaline-phosphatase activity may be due not to bile-duct obstruction, but to an abnormal hepatic over-production of this enzyme. In such a case, markedly raised serum phosphatase values would be found in the absence of any great increase in plasma bilirubin level. Data from 11 patients with this

pattern who were studied at the Johns Hopkins Hospital, Baltimore, are presented, together with comparable data from 54 similar cases reported in the literature. These patients were found to have chronic diffuse infiltration of the liver from such causes as sarcoidosis, tuberculosis, disseminated lupus erythematosus, amyloid disease, and Hodgkin's disease. None of the patients had any evidence of Paget's disease or of metastatic neoplasm, which might confuse the issue. *D. A. K. Black*

1025. **The Metabolism of Folic Acid in Cirrhosis**
J. H. JANDL and A. A. LEAR. *Annals of Internal Medicine* [*Ann. intern. Med.*] **45**, 1027–1044, Dec., 1956. 3 figs., 33 refs.

In view of the possible association between liver damage and the metabolism of substances concerned in normal haematopoiesis the authors, working at Harvard Medical School, Boston, have carried out certain observations on 16 patients with cirrhosis associated with alcoholism, all of whom showed various degrees of anaemia, generally macrocytic and not associated with blood loss. Treatment with folic acid (pteroylglutamic acid:PGA), citrovorum factor (C.F.), and vitamin B_{12} (cyanocobalamin) was tried in these patients and the effects studied.

In 12 patients with varying degrees of haemolytic anaemia associated with a relatively normal bone marrow the administration of PGA and C.F. did not produce a reticulocytosis. The other 4 patients had a megaloblastic marrow and responded to PGA; the serum cyanocobalamin level was relatively normal. The bone-marrow cells resembled strongly those found in pernicious anaemia. No defect of folic acid absorption was found. In the only one of these 4 cases given C.F. there was no response. Tests on normal individuals showed a much greater absorption of synthetic folic acid (PGA) than of natural folic acid from yeast even after preliminary deconjugation. *W. H. Horner Andrews*

1026. **Coagulation Defects in Liver Disease**
D. C. COWLING. *Journal of Clinical Pathology* [*J. clin. Path.*] **9**, 347–350, Nov., 1956. 1 fig., 12 refs.

The author describes investigations carried out at the Postgraduate Medical School of London into the coagulation mechanism in a number of hepatic disorders. Using quantitative techniques he has assayed the blood prothrombin, the plasma components of thromboplastin, and platelets, prothrombin being assayed by the two-stage " area " method, Factor V by the correction of stored oxalated plasma, and Factor VII by the correction of " tromexan " (ethyl biscoumacetate) plasma; the assays of antihaemophilic globulin and of the Christmas factor were dependent on the thromboplastin generation test. The types of liver disease studied included Laënnec's cirrhosis, primary biliary cirrhosis, portal vein thrombosis, acute hepatitis, obstructive jaundice, and amyloid disease.

The author concludes that in liver disease there may be a complex pattern of deficiencies in which the concentrations of Factor V, Factor VII, the Christmas factor, and prothrombin may all be reduced. He found, as have others, that antihaemophilic globulin remains in normal concentration even in the presence of very severe parenchymal liver disease, suggesting that this component may not be produced in the liver.

A. S. Douglas

1027. **Lupoid Hepatitis**
I. R. MACKAY, L. I. TAFT, and D. C. COWLING. *Lancet* [*Lancet*] **2**, 1323–1326, Dec. 29, 1956. 2 figs., 12 refs.

In this paper from the Walter and Eliza Hall Institute of Medical Research and the Royal Melbourne Hospital 7 cases (2 previously reported) of active chronic viral hepatitis are considered, in all of which lupus erythematosus (L.E.) cells were found in the blood. The only other condition in which the authors found L.E. cells was disseminated lupus erythematosus, over 100 samples of blood being tested. Of the 7 patients, 5 were between 16 and 40 years of age, and 6 were females. They presented with typical clinical features of chronic hepatitis and the biochemical findings were those of hepatic insufficiency. Hepatic biopsy demonstrated fibrosis, nodular regeneration, and foci of lymphocytes, plasma cells, and histiocytes. The condition closely resembled that reported by Bearn *et al.* (*Amer. J. Med.*, 1956, **21**, 3; *Abstracts of World Medicine*, 1957, **21**, 97).

In view of the finding of L.E. cells and the presence in most cases of other phenomena suggesting disseminated lupus erythematosus (arthralgia, rashes, haemolytic anaemia, neuropathy) the term " lupoid hepatitis " is proposed for this syndrome. It is suggested that as a result of hepatitis due to viral or other agents autoimmunization against hepatic cells takes place, and an active process of liver damage and repair is started. Cortisone appeared to be of therapeutic value.

W. H. Horner Andrews

1028. **The Diagnostic, Prognostic and Epidemiologic Significance of Serum Glutamic Oxaloacetic Transaminase (SGO-T) Alterations in Acute Hepatitis**
F. WRÓBLEWSKI, G. JERVIS, and J. S. LADUE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **45**, 782–800, Nov., 1956. 19 figs., 8 refs.

The authors have studied the serum glutamic oxaloacetic transaminase (SGO-T) activity in acute hepatitis, using a spectrophotometric method. Although increased SGO-T activity is not specific for liver disease, it may be 20 to 500 times the normal in toxic or viral hepatitis, these values exceeding those reported in any other disorder.

In carbon tetrachloride poisoning in rats and experimental hepatitis in the mouse the SGO-T activity rises approximately in proportion to the degree of liver-cell damage. In viral hepatitis and toxic hepatitis due to drugs in human beings the SGO-T activity rises before abnormalities in liver function are detected by other biochemical tests, the rise coinciding with an increase in the patient's subjective symptoms. Relapse is usually associated with a secondary rise in SGO-T activity. In an epidemic of infective hepatitis in a closed community estimation of the SGO-T activity was of value in detecting subclinical infection.

In " compensated " cirrhosis of the liver the SGO-T activity is normal, but increases with " decompensation ",

as assessed by the appearance of jaundice, ascites, or abdominal pain. The value of the SGO-T activity in the differential diagnosis is limited by the fact that there is some increase in activity in extrahepatic obstructive jaundice and in malignant infiltration of the liver.

P. C. Reynell

1029. **Serum Glutamic Pyruvic Transaminase (SGP-T) in Hepatic Disease: a Preliminary Report**
F. WRÓBLEWSKI and J. S. LADUE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **45**, 801–811, Nov., 1956. 8 figs., 6 refs.

Since the relative concentration of glutamic pyruvic transaminase is greater in liver than in cardiac or skeletal muscle, the authors considered that the activity of the enzyme in the serum (SGP-T) might be a more specific index of liver-cell damage than the serum glutamic oxaloacetic transaminase (SGO-T) activity. Spectrophotometric measurements of SGP-T activity did, in fact, show that there was no appreciable rise after myocardial infarction or in other infectious, neoplastic, reactive, degenerative, or allergic disease states which are sometimes associated with increased SGO-T activity. In 12 patients with viral hepatitis, on the other hand, there was a rise in SGP-T activity which paralleled and exceeded the increase in SGO-T activity. In 8 patients with cirrhosis of the liver SGP-T activity was less than SGO-T activity, although it was above the normal range in 5 cases. SGP-T activity was considerably increased in extrahepatic obstructive jaundice, but in malignant infiltration of the liver it was increased in only 5 of 15 cases, and was always less than the SGO-T activity.

P. C. Reynell

1030. **Circulatory Studies in Liver Cirrhosis.** [In English]
H. KROOK. *Acta medica Scandinavica* [*Acta med. scand.*] **156**, Suppl. 318, 1–160, 1956. 29 figs., bibliography.

1031. **Serum Cholinesterase Activity in Liver Disease.** (Über die Serumcholinesterase-Aktivität bei Lebererkrankungen)
B. KOMMERELL and F. H. FRANKEN. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 1959–1961, Dec. 7, 1956. 21 refs.

The authors have determined the level of serum cholinesterase in a number of patients with various types of liver disease by means of a titration method, the principle of which consists in the titration of the amount of acetic acid produced on splitting a known quantity of acetylcholine at constant temperature, with phenolphthalein as indicator. In most cases the diagnosis was confirmed by liver biopsy examination.

The lowering of the cholinesterase values is explained by the inhibitory effect of the bile pigments on the enzyme, but, it is argued, this cannot be correct in cases in which there is no increase of circulating bilirubin in the serum, as is often the case in cirrhosis. In the authors' cases of hepatitis the cholinesterase activity showed no correlation with the bilirubin level, but both determinations nevertheless gave a good picture of the gravity of the damage to the liver parenchyma. Such damage is even more marked in cases of cirrhosis, where direct deductions of prognostic importance can be drawn, such as, for example, intimations of impending coma.

E. Forrai

INTESTINES

1032. **Fate of the Remaining Rectal Segment after Subtotal Colectomy for Ulcerative Colitis**
C. W. MAYO, O. A. FLY, and M. E. CONNELLY. *Annals of Surgery* [*Ann. Surg.*] **144**, 753–757, Oct., 1956.

The authors have studied the progress of 45 patients subjected to subtotal colectomy for ulcerative colitis at the Mayo Clinic, in all of whom a rectal segment remained more than 90 days after operation. The records showed that in 30 of these cases resection of the rectal stump had been planned for a later date, in 9 ileorectal anastomosis was to be carried out later, if possible, and in 6 no definite plan for the future had been made.

In 21 of the first group of 30 cases the rectal segment was eventually excised. Of the remaining 9 patients who had not been operated on for removal of the rectal stump, 2 were intending to undergo resection, 2 had comparatively mild symptoms (although protoscopic examination showed activity in one and a persistent perineal fistula in the other), one had extensive peritoneal metastases from a previously treated carcinoma of the colon and resection had to be abandoned, and one had developed tuberculosis. Only 2 of the 9 patients complained of minimal rectal discharge, and in one of these examination revealed that the rectum was a "scarred tube" which could not be "utilized satisfactorily for ileosigmoidostomy".

Of the 9 cases in which it had been hoped that ileorectal anastomosis might be possible later, only one was operated on in this way and the postoperative course was stormy. Resection was performed in one case, in the remainder the rectal stump being still present at the time of follow-up. Of these latter 7 cases, 5 showed evidence of active ulcerative disease in the rectum; only in 2 cases did the rectum appear free from disease.

In 3 of the 6 cases in which operation had not been planned, resection of the rectal segment was subsequently carried out; in the 3 other cases the rectal segment remained, with active disease.

The authors conclude that if ileorectal anastomosis is not possible at the time of colectomy, as much of the rectum as possible should be removed at the initial operation and the rest later.

T. D. Kellock

1033. **Staphylococcal Diarrhoea. With an Account of Two Outbreaks in the Same Hospital**
J. COOK, C. ELLIOTT, A. ELLIOT-SMITH, B. R. FRISBY, and A. M. N. GARDNER. *British Medical Journal* [*Brit. med. J.*] **1**, 542–547, March 9, 1957. 44 refs.

Correction.—The investigation into tea-drinking and gastritis described in Abstract 545 in the March issue was carried out at the West Middlesex Hospital, Isleworth, and not at the Central Middlesex Hospital as stated.—EDITOR.

Cardiovascular System

1034. **Observations on Some Possible Precursors of Essential Hypertension and Coronary Artery Disease: V. Hypercholesteremia in Healthy Young Adults**
C. B. THOMAS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 389–396, Oct., 1956. 7 figs., 6 refs.

At Johns Hopkins Hospital, Baltimore, the serum cholesterol concentration was measured in 612 healthy medical students and was found to be abnormally high (more than 300 mg. per 100 ml.) in 53 (9%). An enquiry into the family history of these 53 students revealed that about one-third (32%) of them had a parent (usually the father) with coronary arterial disease, compared with such a finding in only 11·8% of the 559 students in whom the serum cholesterol level was within normal limits. Further, there was a significantly higher incidence of severe or fatal disorders among the parents of the former group compared with those of the latter. It was noted that a slight increase in the mean cholesterol values occurred with increasing age among the 559 students with normal serum cholesterol concentration, amounting in this series to 2·88 mg. per 100 ml. per year, but there were wide individual variations. In 11 subjects whose cholesterol levels were determined on two occasions at 4 to 7 years' interval, only 2 showed an increase and this was slight.

It is concluded that (1) the hypercholesterolaemic trait in young adults is linked with a familial tendency to cardiovascular, especially coronary arterial, disease; (2) a metabolic defect is probably involved; (3) a person with such a trait can be detected by periodic measurements of the serum cholesterol level, but, the author adds, while measures designed to maintain a normal blood cholesterol level in these individuals might alter the subsequent disease pattern, they would probably have little effect on the fundamental metabolic defect.

Gerald R. Graham

1035. **Massive Thrombotic Occlusion of the Large Pulmonary Arteries**
K. P. BALL, J. F. GOODWIN, and C. V. HARRISON. *Circulation* [*Circulation (N.Y.)*] **14**, 766–783, Nov., 1956. 10 figs., 29 refs.

The authors of this paper from the Central Middlesex Hospital and the Postgraduate Medical School (Hammersmith Hospital), London, are of the opinion that massive thrombosis of the large pulmonary arteries is infrequently considered in the differential diagnosis of obscure cases of right-sided heart failure. They now present 23 such cases not due to acute massive embolism, 9 of which were seen during life. The cases were divided into (1) those in which the thrombosis occurred without associated disease, and (2) those in which other diseases were present, the most common of these being mitral stenosis (6 cases). The main symptoms were those of right heart failure and low cardiac output. Radiologically, there was a combination of clear lung fields and enlarged pulmonary arteries. The authors consider that the diagnosis of pulmonary arterial thrombosis should be considered whenever a patient presents with unexplained congestive failure, dyspnoea, fainting, repeated attacks of pulmonary infarction, or pain in the chest—especially in a case of mitral stenosis.

In discussing the aetiology of the condition it is pointed out that in most cases the thrombosis was secondary to embolism, but in 7 cases it was considered to have arisen primarily in the pulmonary artery. The treatment advised is administration of anticoagulants or, in the last resort, ligation of the inferior vena cava.

J. B. Wilson

1036. **The Use of Molar Sodium Lactate in Certain Arrhythmias Complicating Intracardiac Surgery**
W. S. BLAKEMORE, H. F. ZINSSER, C. K. KIRBY, S. BELLET, and J. JOHNSON. *Annals of Surgery* [*Ann. Surg.*] **144**, 511–517, Oct. [received Dec.], 1956. 3 figs., 7 refs.

In 3 patients suffering respectively from atrial septal defect, calcific aortic stenosis, and mitral regurgitation who developed " bradycardia and ineffective heart beat " due to ventricular fibrillation or slow idioventricular rhythms during intracardiac surgery at the Hospital of the University of Pennsylvania, Philadelphia, the intravenous infusion of molar sodium lactate was helpful in resuscitation and in the restoration of sinus rhythm. Other measures concurrently employed included electric shock and the injection of various drugs. The mode of action of sodium lactate in cases of arrhythmia has not yet been clarified, but its complex effects on the serum electrolytes, especially potassium, are briefly discussed.

A. Schott

1037. **Cerebral Abscess in Cyanotic Congenital Heart-disease**
M. CAMPBELL. *Lancet* [*Lancet*] **1**, 111–115, Jan. 19, 1957. 22 refs.

Among the 800 or so cases of cyanotic congenital heart disease seen at Guy's Hospital, London, during the past decade were found 14 proved cases and one probable case of brain abscess. The patients were aged between 3 and 25 years. All had central cyanosis and a right-to-left shunt: 11 had Fallot's tetralogy, 2 had additional pulmonary atresia, and 2 transposition of great vessels. In 11 cases there was a solitary cerebral abscess, the abscess sites being widely scattered in the brain. Headaches and drowsiness were not often prominent, and fits, hemiplegia, or homonymous hemianopia often occurred with little warning. Nine of the patients died, and only one of these had undergone a cardiac operation. Of the 6 patients who recovered, 4 had undergone a cardiac operation, which probably helped them later to

survive the abscess. One patient developed an abscess or infected embolism 6 weeks after cardiac catheterization. Most patients had no sign of infection elsewhere; middle-ear disease was present in 2, but was not clearly responsible for the abscess.

The author concludes that cerebral abscess is commoner in patients with cyanotic congenital heart disease than in others; in such patients it is a greater hazard than bacterial endocarditis. He considers that secondary infection of a cerebral thrombus is a frequent cause, although paradoxical embolism probably accounts for some cases. *D. Emslie-Smith*

1038. **Repair of Interatrial Septal Defects by a Modified Sondergaard Technique (Circumclusion)**
L. H. Bosher. *Surgery* [*Surgery*] **41**, 129–145, Jan., 1957. 14 figs., 26 refs.

ENDOCARDITIS

1039. **A Contribution to the Study of Parietal Fibroplastic Endocarditis with Eosinophilia (Loeffler's Endocarditis).** (Contribution à l'étude de l'endocardite pariétale fibroplastique avec éosinophilie sanguine (endocardite de Loëffler))
A. Gerbaux, M. Ben-Naceur, J. De Brux, and J. Lenègre. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **49**, 689–715, Aug. [received Nov.], 1956. 8 figs., bibliography.

The authors describe, from the Hôpital Boucicaut, Paris, 2 cases of cardiovascular disease associated with a high degree of eosinophilia which, in spite of treatment, progressed rapidly to cardiac failure and death within a few months of onset. At necropsy a severe degree of endocardial fibrosis extending into the myocardium of the ventricles was found. Investigations for parasitic infestation gave negative results (neither of the patients had been to the tropics), and treatment with ACTH and cortisone, though reducing the percentage of circulating eosinophils, was ineffective.

These are considered to be cases of non-specific endocardial fibrosis of the type described by Loeffler. The aetiology of the condition is discussed on the basis of similar cases reported in the literature, the roles of infection, allergy, and possibly periarteritis nodosa in causation being considered, but no firm conclusion is reached. *J. Robertson Sinton*

1040. **Teeth, *Streptococcus viridans*, and Subacute Bacterial Endocarditis**
F. G. Hobson and B. E. Juel-Jensen. *British Medical Journal* [*Brit. med. J.*] **2**, 1501–1505, Dec. 29, 1956. 11 refs.

Between 1945 and 1955, 59 cases of subacute bacterial endocarditis were admitted to the Radcliffe Infirmary, Oxford, the infection in 43 being due to *Streptococcus viridans* and in 16 to other organisms. The dosage of penicillin given in these cases increased during the 10-year period, but the mortality (about 25%) did not fall. A study of the records concerning the dental state of the patients revealed that none of those with subacute bacterial endocarditis due to *Strep. viridans* was edentulous. In some 25% of the patients in this series relapse occurred within a few months or years of apparent cure, and the authors believe that the main cause of this was failure to eliminate the primary dental focus. They contend that removal of all teeth should be an essential part of the treatment of subacute bacterial endocarditis due to *Strep. viridans*. They did not find that there was any uniform practice in the provision of penicillin "cover" for dental extraction. In 3 of their cases given 8 to 12 mega units of soluble penicillin a day *Strep. viridans* was cultured from a specimen of blood after dental extraction, and in 6 other cases given a similar dosage of penicillin a very heavy growth of this organism was obtained from both "good" and "bad" extracted teeth.

The authors recommend that in cases of heart disease in which subacute bacterial endocarditis may develop one mega unit of soluble penicillin should be given 30 minutes before removal of one or 2 teeth, followed by one mega unit the same night and thereafter 12-hourly for 3 days. In established cases or cases in relapse one mega unit should be given 6-hourly for 5 days after operation. *G. S. Crockett*

CHRONIC VALVULAR DISEASE

1041. **Percutaneous Left Ventricular Puncture in the Assessment of Aortic Stenosis**
R. Brock, B. B. Milstein, and D. N. Ross. *Thorax* [*Thorax*] **11**, 163–171, Sept., 1956. 9 figs., 11 refs.

Measurement of the pressure gradient across the aortic valve is important in assessing the degree of aortic valve disease and in the selection of cases for valvotomy. The authors, writing from the Brompton and Guy's Hospitals, London, describe a method whereby this information can be obtained preoperatively by means of left ventricular puncture through the intact chest wall. They point out that left atrial puncture had previously been used for this purpose, but was abandoned because complications such as pneumothorax, haemothorax, haemoptysis, and haemopericardium were frequent; in one of the authors' small series (24 cases) examined by that method there were 3 deaths which were possibly precipitated by the procedure. The technique of left ventricular puncture is described. The axis of the outflow tract of the left ventricle corresponds with a line drawn from the apex of the heart to the right 2nd costochondral junction and inclined backwards at an angle of about 35 degrees to the sternum. A needle inserted in this line is more likely to enter the left ventricular chamber than one passing across the outflow tract, and is less likely to damage the coronary vessels.

The authors have now employed the technique in 24 cases, and have found it simple, safe, and not disturbing to the patient; there were no serious complications. Simultaneous left ventricular and brachial arterial pressure tracings were recorded, and all results are tabulated. In 12 cases subsequently treated surgically the pressures

recorded at operation were generally found to agree closely with those obtained preoperatively by left ventricular puncture. Studies were made of the electrocardiogram, blood pressure, pulse rate, and cardiac output before and during the procedure. The only changes in cardiac rhythm observed were ectopic ventricular beats, and there was no significant haemodynamic change which might have invalidated the results. The possibility that ventricular fibrillation and cardiac arrest might occur during the procedure was borne in mind and instruments were kept in readiness for immediate thoracotomy, cardiac resuscitation, and aortic valvotomy.

The authors suggest that the technique may also be of value in the investigation of mitral-valve disease. They have used it, combined with per-bronchoscopic left atrial puncture, in the measurement of mitral-valve gradients, and consider it less disturbing to the patient than catheterization of the left ventricle via a left atrial puncture through the posterior chest wall.

F. J. Sambrook Gowar

1042. **A Discussion of the Haemodynamic Criteria of Tricuspid Insufficiency.** (Discussion des critères hémodynamiques de l'insuffisance tricuspidienne)
A. Tourniaire, J. Blum, M. Tartulier, and F. Deyrieux. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **49**, 785–797, Sept., 1956. 8 figs., 31 refs.

The authors discuss the haemodynamics of tricuspid incompetence with special reference to 15 cases of the condition seen at the Hôpital Saint-Joseph, Lyons. The diagnosis rested upon the combined presence of a number of clinical signs, of which systolic pulsation of the jugular veins (seen in all cases) and of the veins of the liver (seen in 14) were the chief, although in only 4 cases was a systolic murmur heard at the tricuspid area; in 12 cases there was atrial fibrillation. Cardiac catheterization was performed in all 15 cases.

In 7 cases, all in fibrillation, the right atrial pressure tracing showed an obvious regurgitation wave, a rise in pressure which was synchronous with ventricular systole beginning 0·05 to 0·08 second after the R wave of the electrocardiogram. The peak atrial pressure reached in this regurgitation lay between 12 and 30 mm. Hg, being between one-quarter and one-half of the right ventricular systolic pressure. In the 3 cases showing normal rhythm the atrial regurgitation wave began appreciably later than the ventricular systolic wave, the lag being 0·02 to 0·11 second and causing possible confusion with an early V wave. The pattern in the remaining 5 cases was similar although modified by the presence of atrial fibrillation; it showed an absent " a " wave, well formed " c " wave, poor X descent, positive regurgitation wave, and deep Y descent. When diastole was short the rise from Y descent to " c " wave was abrupt; when diastole was longer a gradually rising line linked Y and " c ". The regurgitation wave reached a value between 15 and 35 mm. Hg.

The authors point out that atrial fibrillation, heart failure, and constrictive pericarditis may all simulate the pattern just described. However, in tricuspid insufficiency the regurgitation wave is accentuated on inspiration or after long diastolic pauses. Essentially, the regurgitation wave reaches a peak exceeding one-quarter of the value of right ventricular systolic pressure, and is clearly greater than the right ventricular filling pressure. The present findings are discussed in comparison with those of other cardiologists. *J. A. Cosh*

1043. **Diagnosis of Mitral Regurgitation by Cardioangiography**
P. W. Smith, H. A. Cregg, and K. P. Klassen. *Circulation* [*Circulation* (*N.Y.*)] **14**, 847–853, Nov., 1956. 9 figs., 11 refs.

As the surgical methods now available can relieve pure mitral valvular stenosis but not those lesions in which regurgitation predominates, it is highly desirable to differentiate these conditions preoperatively. Angiocardiography has proved unsatisfactory because the contrast medium is diluted or retained in the enlarged left atrium. The authors' method of cardioangiography, as employed at the Ohio State University Health Center, Columbus, Ohio, is to inject diodone directly into the left ventricle by a subxiphoid puncture under local analgesia. Serial radiographs are then taken in the right posterior oblique position, in which the left main-stem bronchus should mark the superior border of the left atrium. The reliability of the method has been demonstrated in experiments on dogs in which diodone was injected before and after mitral incompetence was produced by injury to the mitral valve. After injury there was regurgitation of the contrast medium into the left atrium and pulmonary veins.

In the authors' present series of 20 cases there were no deaths; one patient who developed ventricular arrest following injection of medium into the left coronary artery recovered after direct cardiac massage. Of 6 of the cases subsequently examined at operation or necropsy, the findings in 5 confirmed the results of the cardioangiographic studies. *D. Goldman*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1044. **Endocrine Aspects of Coronary Sclerosis**
M. F. Oliver and G. S. Boyd. *Lancet* [*Lancet*] **2**, 1273–1276, Dec. 22, 1956. 2 figs., bibliography.

The fact that when coronary sclerosis produces symptoms there is a rise in plasma level of cholesterol and of the beta and low-density lipoproteins " has emphasized the need for investigation of dietary and endocrine influences on lipid metabolism ". This the authors have undertaken at the Royal Infirmary, Edinburgh, where they studied the effects of various hormones on the plasma cholesterol, the total cholesterol:phospholipid (C:P) ratio, and the alpha- and beta-lipoprotein cholesterol in both healthy and hypercholesterolaemic subjects.

In hypercholesterolaemic men with coronary arterial disease it was found that administration of corticotrophin, cortisone, L-thyroxine, L-triiodothyronine, triiodothyroacetic acid, and synthetic and natural oestrogens signi-

ficantly depressed the plasma cholesterol level, the C:P ratio, and the beta-lipoprotein cholesterol level, whereas it caused a rise in level of alpha-lipoprotein cholesterol. Similar but less marked changes were noted when progesterone was given. Methyl testosterone, on the other hand, caused a rise in plasma cholesterol and beta-lipoprotein cholesterol levels and a fall in that of alpha-lipoprotein cholesterol. No significant changes followed administration of growth hormone and insulin to normocholesterolaemic men, whereas after giving glucagon there was a slight elevation of plasma cholesterol and beta-lipoprotein cholesterol levels and a reduction in alpha-lipoprotein cholesterol level. The period of administration of the sex hormones rarely exceeded 1 to 3 weeks except in the case of ethinyl-oestradiol.

The authors conclude that clinical coronary arterial disease may in part be caused by endocrine imbalance, and the possible mechanisms of this are discussed from the following aspects: (1) the effects of hormones on the levels of circulating lipids; (2) the effects of hormones on blood coagulation and fibrinolytic activity; and (3) their influence on certain types of tissue reactions.

J. Warwick Buckler

1045. **Age, Sex, Serum Lipids, and Coronary Atherosclerosis**

D. ADLERSBERG, L. E. SCHAEFER, A. G. STEINBERG, and CHUN-I WANG. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 619–622, Oct. 13, 1956. 2 figs., 18 refs.

There is increasing evidence that atherosclerosis is fundamentally a metabolic disorder due mainly to an inborn error in the metabolism of lipids and lipoproteins, occurring in genetically predisposed subjects and modified by many environmental influences. In order to obtain a more reliable impression of this disorder the authors, at the Mount Sinai Hospital, New York, estimated the serum cholesterol and phospholipid levels in 1,200 apparently healthy males and females between 2 and 77 years of age and belonging to families selected at random from the industrial population of Staten Island; 98% were of white race and 2% negro. The average serum cholesterol level of males was found to rise suddenly after the age of 23–27 years from about 190 mg. per 100 ml., reaching 243 mg. per 100 ml. in the age group 28–32 years. For females in corresponding age groups the figure remained around 200 mg. per 100 ml. The same statistically significant differences were found in the serum phospholipid values. Both the serum cholesterol and phospholipid levels afterwards remained fairly constantly the same in the whole range of the higher age groups in men. In women, however, the serum cholesterol level rose gradually to become much higher after the age of 48, reaching a level of 285·5 mg. per 100 ml. in the age group 53–57 years; it remained at this level throughout the higher age groups. A similar rise in phospholipid level was maintained in the women.

The differences in the age trends between males and females were related to the well-known experience that men constitute about 90% of those suffering from coronary arterial disease under the age of 50, and that cardiac infarction occurs at an earlier average age in men than in women. After the age of 50, however, the proportion of females suffering from coronary heart disease increases substantially.

Z. A. Leitner

1046. **Long-term Effect of Dried Thyroid on Serum-lipoprotein and Serum-cholesterol Levels**

B. STRISOWER, J. W. GOFMAN, E. F. GALIONI, J. H. RUBINGER, J. POUTEAU, and P. GUZVICH. *Lancet* [*Lancet*] **1**, 120–123, Jan. 19, 1957. 2 figs., 11 refs.

In a prolonged trial (2 years) of the effect of thyroid extract on the serum lipid levels, carried out at Stockton State Hospital, California, dried thyroid was given to 60 schizophrenic but otherwise healthy patients, 30 women aged 27 to 56 (mean 39·6) years and 30 men aged 25 to 57 (mean 40·3) years. For the first 30 weeks a dose of 195 mg. daily was given. In response to this dosage there was a fall of the mean serum total cholesterol level from 216 to 157 mg. per 100 ml., of the S_f 0–12 lipoprotein content from 354 to 256 mg. per 100 ml., and of S_f12–20 lipoprotein content from 76 to 44 mg. per 100 ml. The higher the initial levels, the greater was the fall during thyroid administration.

It was noted that the cholesterol and lipoprotein concentrations tended to rise during this period, though they declined once more when the dose was increased to 260 mg. daily (for 39 weeks) and later to 325 mg. daily (for 36 weeks). This " escape " during administration of 195 mg. of dried thyroid daily is attributed to diminished endogenous production of thyroid hormone. As expected, immediately after therapy was stopped the serum cholesterol and lipoprotein concentrations rose to above the pre-treatment levels, presumably because of the combined effect of withdrawal of exogenous thyroid hormone and the continuing depression of endogenous thyroid secretion, but then gradually fell again towards pre-treatment levels, presumably as the production of endogenous hormone increased again. No significant effect on the body weight of these patients was observed. It is suggested that dried thyroid might be a useful prophylactic agent against coronary arterial disease.

Robert de Mowbray

1047. **The Influence of Triiodothyroacetic Acid on the Circulating Lipids and Lipoproteins in Euthyroid Men with Coronary Disease**

M. F. OLIVER and G. S. BOYD. *Lancet* [*Lancet*] **1**, 124–126, Jan. 19, 1957. 2 figs., 21 refs.

At the Royal Infirmary, Edinburgh, triiodothyroacetic acid (" triac ") was given to 12 men aged 33 to 49 (mean 42) years, with hypercholesterolaemia but normal thyroid function, who had suffered myocardial infarction (confirmed by electrocardiography) more than 9 months previously but who had since returned to work.

In 6 of the cases doses of triac increasing gradually from 0·5 to 4 mg. daily produced no significant changes in the plasma cholesterol values until 3 mg. daily was given, when the plasma total cholesterol level, the cholesterol:phospholipid ratio, and the proportion of cholesterol attached to beta lipoprotein all showed a reduction. In the other 6 cases, in which initial doses of 3

to 5 mg. daily were given, similar lipid changes developed after a dose of 3 mg. had been given for one month. The basal metabolic rate (B.M.R.) was not raised in the majority of cases. The depression of the plasma cholesterol level could not be maintained over long periods, even when the dose was increased, for larger doses (up to 5 mg. daily) were no more effective than smaller ones and were in any case more liable to induce anginal pain; in fact, in 3 of the 12 men given this dosage the exercise tolerance diminished from a previously normal level and angina developed or was greatly aggravated (in one of these patients the B.M.R. was raised). The optimum dose of 3 to 4 mg. daily is six to eight times that required by hypothyroid patients. The authors conclude that triac may not prove suitable for the long-term control of hypercholesterolaemia in patients with clinical coronary disease. *Robert de Mowbray*

1048. **Some Physico-chemical Properties of the Blood in Disturbances of the Coronary Circulation.** (О некоторых физико-химических свойствах крови при нарушении венечного кровообращения)
V. M. PANCHENKO. *Терапевтический Архив* [*Ter. Arkh.*] **28**, 10–16, No. 7, 1956. 9 refs.

While much work has been done on myocardial infarction and the mortality from this cause has been considerably reduced as the result of improved diagnosis and new methods of treatment and rehabilitation, it is the author's impression that the aetiology and pathology, particularly the process of thrombus formation, have been somewhat neglected.

The investigations here reported from the Central Institute of Postgraduate Medicine, Moscow, were made on 172 patients—50 with angina, 32 with old myocardial infarction and angina, and 90 with recent infarction. In 107 cases the condition was linked with atherosclerotic cardiosclerosis, in 56 there was a background of hypertension, in 8 a neurosis, and in one rheumatism. The findings were compared with those in a group of 48 individuals over the age of 40 who served as controls. Of the various factors concerned in thrombus formation the only one showing a significant change in relation to recent infarction was the plasma fibrinogen content, which in 93% of cases was increased immediately after the episode and then gradually returned towards the normal level coincident with repair, this process extending over one to 3 months. An increase in the prothrombin level was observed in only one-third of the acute cases of infarction. *R. Crawford*

1049. **Serum Glutamic–Oxalacetic Transaminase in Coronary Artery Disease. A Review of 201 Cases**
B. H. OSTROW, D. STEINBERG, H. E. TICKTIN, G. N. POLIS, and J. M. EVANS. *Circulation* [*Circulation (N.Y.)*] **14**, 790–799, Nov., 1956. 6 figs., 17 refs.

The results of serial serum glutamic–oxalacetic transaminase (G.O.T.) assays in 201 cases in which coronary arterial disease was suspected are reported from the George Washington University Medical School, Washington, D.C., and the National Institutes of Health, Bethesda, Maryland. The G.O.T. was estimated on at least 5 successive days after the onset of symptoms. Other investigations included electrocardiographic (ECG) and complete clinical examinations, the results of which were correlated with the G.O.T. readings. Elevated G.O.T. values were found in 95% of the cases. Correlation between raised G.O.T. level and clinical–ECG findings was obtained in 88% of the whole series. In 18 cases of acute myocardial necrosis which came to necropsy the correlation was 100%. However, in 18 cases where the clinical–ECG diagnosis was uncertain or negative for infarction the G.O.T. level was high, and 6 of these cases were found to have non-cardiac disease.

The authors conclude that determination of the serum G.O.T. level provides a useful additional aid in the diagnosis of myocardial infarction. *J. B. Wilson*

1050. **Effects of Cortisone on Metabolic Responses in Myocardial Infarction**
G. G. BERGY, R. W. BURROUGHS, and R. A. BRUCE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 513–517, Nov., 1956. 3 figs., 5 refs.

At King County Hospital (University of Washington School of Medicine), Seattle, 5 unselected patients with acute myocardial infarction were treated with 300 mg. of cortisone daily by mouth for the first 12 days after the clinical onset of the infarction. The usual supportive treatment was also given, but no anticoagulants were administered.

Two severely ill patients in heart failure with extensive infarction died on the 10th and 12th days respectively after admission; in these cases the sodium and water retention had been moderate. No sodium or water imbalance occurred in the other 3 patients, although 2 of them developed congestive heart failure. There was no evidence that the course of the disease, morbidity, mortality, or the blood pressure were influenced by cortisone.

[The small number of patients and the difference in their clinical condition on admission make these findings quite inconclusive.] *Gerald R. Graham*

1051. **Pathogenesis of Cardiac Rupture due to Myocardial Infarction. A Study of Twenty-six Cases**
J. H. LUNSETH and M. RUWALDT. *Diseases of the Chest* [*Dis. Chest*] **30**, 499–507, Nov., 1956. 5 figs., 14 refs.

The authors have made a detailed study of 26 cases of myocardial infarction with cardiac rupture coming to necropsy at Milwaukee (Wisconsin) County Hospital in an attempt to determine the aetiological factors involved and the potential role played by intramural haemorrhage. In all cases the site of rupture was within the area of infarction. A major factor in producing the rupture was considered to be penetration of the wall by a dissecting haematoma, in a similar manner to that occurring in dissecting aortic aneurysm. Contrary to accepted opinion the degree and extent of myocardial fibrosis and the granulocytic exudation were thought to play only a small part, while no evidence was obtained that thrombosis of the Thebesian vessels played any part, in the aetiology of the cardiac rupture. *J. B. Wilson*

HEART FAILURE

1052. **Oxygen Starvation in Chronic Cardiac Insufficiency.** (Кислородное голодание при хронической сердечной недостаточности)
L. M. GEORGIEVSKAYA. *Терапевтический Архив* [*Ter. Arkh.*] **28**, 16–26, No. 7, 1956. 5 figs., 37 refs.

The author presents, from the first Pavlov Medical Institute, Leningrad, the results of a comprehensive and well documented study of the blood gases in 26 healthy subjects (29 investigations) and 51 cases of cardiac insufficiency of all degrees (70 investigations). The conclusions may be summarized as follows. (1) The oxygen saturation of arterial blood in cardiac patients without obvious involvement of the lungs is slightly below normal. (2) In cardiac insufficiency of Grade III the presence of arterial hypoxaemia is shown by significant changes in the lungs and the high position of the diaphragm. (3) With increased cardiac insufficiency the arteriovenous difference in the degree of oxygen saturation and also the utilization of oxygen both fall as a result of the diminishing saturation of venous blood. (4) Oxygen tension in arterial blood and the average capillary tension are lowered somewhat in Grade-II insufficiency, but rise again to near normal level in that of Grade III. (5) In the majority of cases the curve of combined oxygen shows a shift to the right in relation to the development of non-gaseous acidosis. (6) Carbon dioxide tension in venous blood increases with an increase in cardiac insufficiency, the venoso-arterial difference in CO_2 tension being thereby increased; at the same time the CO_2 tension in the arterial blood falls. (7) Increased production of carbon dioxide counteracts the increasing non-gaseous acidosis that accompanies increasing insufficiency, but in the process the buffer properties of the blood are reduced, the alkali reserve is diminished, and the curve of combined CO_2 falls.

(8) After copious diuresis produced by mercurials and after removal of ascitic fluid a normal degree of oxygen saturation is re-established. At the same time the arteriovenous difference in oxygen saturation and the venosoarterial difference in CO_2 saturation rise, mainly on account of changes in the gases in the arterial blood. The curve of CO_2 saturation falls after administration of mercurials, and the *p*H of both arterial and venous blood moves towards acidosis. If there is excessive action of mercurial diuretics excessive quantities of fluid entering the circulation may cause a condition of uncompensated acidosis, with considerable change in the *p*H. (9) With improvement in the cardiac condition the alkali reserve increases by reason of the compensatory function of the kidney, which ensures the retention of elements in the blood. (10) The breathlessness of the cardiac patient is, in the majority of cases, an expression not of respiratory insufficiency in the sense of hypoxaemia, but of a compensatory factor in the struggle of the organism with acidosis. (11) Acidosis in cardiac insufficiency develops as a result of the inadequate supply of oxygen to the tissues arising from the haemodynamic disturbances, and not as a result of inadequacy of the physical and physico-chemical systems and disturbance of the permeability of the capillary and tissue membranes. (12) The supply of oxygen to the tissues is diminished only in the event of disturbance in their blood supply.

R. Crawford

LYMPHATIC CIRCULATION

1053. **Lymphatic Circulation Studied with Radioactive Plasma Protein**
G. W. TAYLOR, J. B. KINMONTH, E. ROLLINSON, J. ROTBLAT, and G. E. FRANCIS. *British Medical Journal* [*Brit. med. J.*] **1**, 133–137, Jan. 9, 1957. 4 figs., 12 refs.

In a study at St. Bartholomew's Hospital, London, of the lymphatic circulation plasma protein labelled with radioactive iodine (^{131}I) (R.P.P.) was injected subcutaneously in order to determine (1) the mode of removal of extravascular protein molecules; (2) differences in absorption between healthy and lymphoedematous subjects; and (3) whether the rate of removal from subcutaneous tissues could be used as a test of lymphatic function in clinical practice. Determinations were made on 6 healthy and 10 lymphoedematous subjects, on healthy rabbits, and on animals with a limb made oedematous by acute lymphatic transection. Not more than 0·1 ml., usually containing 100 microcuries of ^{131}I, was injected at any one site. Where a larger volume had to be used because of low specific activity of the R.P.P., several sites were used but grouped closely together. In human subjects activity in the area of the injection was best observed by using a shielded Geiger–Müller tube held 22 cm. from the skin. In rabbits a small unshielded Geiger–Müller tube in a thin brass case was held parallel to the paw with its axis about 2 cm. from the skin.

In human subjects local counting over the injection site showed that (1) there was a wide subcutaneous diffusion of R.P.P. around the site, which was influenced by gravity and was greater in the lymphoedematous subjects; (2) in healthy subjects the removal rate was increased by physical activity; and (3) the removal rate was greater in normal active subjects than in the lymphoedematous. In rabbits it was found that the R.P.P. removed from the paw was being dumped at the site of transection, so that a true removal rate from the limb could not be determined.

In measuring the activity of blood specimens it was found that a correction had to be applied to the readings because of the rapid absorption of ^{131}I iodide present in trace quantities in the injection solution. This impurity resulted in an initial small rise and flattening of the curve. These measurements showed that (1) there was a delay of 0·5 to 3·25 hours between injection of R.P.P. and detection in the blood; (2) patients with severe lymphoedema showed a greater delay than healthy subjects; (3) healthy subjects showed a greater initial rate of rise than lymphoedematous patients; and (4) physical activity in healthy subjects increased the initial rate of rise. In rabbits the main difference was that after lymphatic transection R.P.P. could be detected in the blood immediately following injection.

The authors conclude that subcutaneously injected R.P.P. is removed by the lymphatic route rather than being absorbed directly into the blood through the capillary walls, such direct absorption occurring only after acute traumatic destruction of the lymphatic pathway. They suggest that the method can be used as a test of lymphatic function, and is probably useful for research but too costly and time-consuming for routine clinical purposes.

A useful survey of earlier work is given.

I. M. Rollo

BLOOD VESSELS

1054. **Hemodynamic and Clinical Appraisal of Coarctation Four to Seven Years after Resection and End-to-end Anastomosis of the Aorta**

J. L. WRIGHT, H. B. BURCHELL, E. H. WOOD, E. A. HINES, and O. T. CLAGETT. *Circulation* [*Circulation (N.Y.)*] **14**, 806–814, Nov., 1956. 6 figs., 14 refs.

At the Mayo Clinic 10 patients (5 male and 5 female) who had undergone resection and end-to-end anastomosis of the aorta for coarctation 4 to 7 years previously were studied extensively in order to assess the long-term results of the operation and also at the same time to compare the haemodynamic findings with those observed before and immediately after operation.

All the patients were well, and 2 had had uneventful pregnancies. The preoperative systolic murmur present in all 10 cases was absent in 3 and diminished in a further 3. The results of simple blood counts and urine analyses were all normal. Electrocardiographic evidence of decreased ventricular hypertrophy was present in only one case. Notching of the ribs, which had been present in 9 patients before operation, was diminished in one and had disappeared in another who had been 12 years old at the time of operation. There was a minor decrease in heart size in 5 patients and marked decrease in one. No patient had residual severe hypertension although there was a moderate degree of increased tension in 4 cases. The most striking change was that the radial and femoral arterial pressures were within normal range in the majority of patients. Cardiac output was within normal limits in all cases, and peripheral arterial resistance was slightly raised in 3 patients and normal in the others. A slight to moderate degree of residual coarctation persisted in 5 cases.

D. Goldman

1055. **Intra-arterial Oxygen in Peripheral Vascular Disease**

R. J. MARSHALL and R. F. WHELAN. *British Medical Journal* [*Brit. med. J.*] **2**, 1448–1451, Dec. 22, 1956. 8 figs., 11 refs.

The observation that injection of small quantities of oxygen or of other gases into the brachial artery of a normal subject is followed by vasodilatation in the hand and forearm persisting for an hour or more has suggested to the authors a possible therapeutic application in patients with ischaemic disorders of the limbs. This has led them to study the local circulatory effects of intra-arterial injections of oxygen in 18 cases of peripheral vascular disease at the Queen's University of Belfast. The investigations were carried out at a room temperature of 20° to 24° C. The patient rested on a couch for at least an hour before observations were made. In the upper limb injections were made into the brachial artery in the antecubital fossa; in the lower limb into the femoral artery in the groin, the limb injected being raised slightly. A continuous infusion of 0·9% saline solution into the artery was maintained by means of a mechanically driven syringe, and the gaseous oxygen was added slowly to the stream of saline through a side-arm in the connecting tube. In most cases the injection of oxygen resulted in an increase in blood flow lasting for 24 to 60 hours. Injections of tolazoline, hydrallazine, and "dilatal" (phenyl-*iso*-butyl-n-*p*-hydroxyephedrine) caused only relatively transient increases in the blood flow.

Intra-arterial injection of oxygen is considered a safe procedure provided certain precautions are taken and it is not used for patients with a very low resting blood flow or in whom occlusion of a major blood vessel has recently occurred. Although occasionally there was a paradoxical effect such as occurs with any other potent vasodilator, it is concluded that the injection of oxygen is preferable to other methods in the treatment of peripheral vascular disease.

Leon Gillis

1056. **Oral Dibenyline in Distal Senile Obliterative Arteritis**

A. M. BOYD. *Lancet* [*Lancet*] **2**, 869–871, Oct. 27, 1956. 2 refs.

It is pointed out in this paper from the University of Manchester that vasodilators may be expected to ameliorate symptoms of peripheral vascular occlusion only so long as the main artery to the limb—the main pressure feed—is intact; thus they may be more effective in distal obliterative disease. Dibenyline, N-phenoxy-*iso*propyl-N-benzyl-β-chloroethylamine hydrochloride, which has a highly specific action, blocking the peripheral motor action of adrenaline, was tried in 30 patients with mild, moderate, or severe symptoms of Raynaud's disease resulting from digital arterial narrowing or thrombosis. The initial dosage was 10 mg. at night for 3 nights, followed by 10 mg. night and morning; at the end of a week the dosage was increased to 10 mg. three times a day and later still, if necessary, to a maximum of 60 mg. daily.

As might be expected relief was most marked in patients with mild symptoms. Undesirable side-effects, such as drowsiness, dizziness, and stuffiness of the nose, were noted in 12 patients. The author concludes that administration of dibenyline is the treatment of choice in patients with mild symptoms and offers an alternative to sympathectomy in many with moderately severe symptoms.

F. B. Cockett

1057. **Poststenotic Dilatation (Aneurysm) of the Subclavian Artery Associated with Cervical Rib. Report of Two Cases Visualized by Angiocardiography**

I. STEINBERG. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 242–244, Feb. 7, 1957. 2 figs., 13 refs.

Haematology

1058. **The Pathogenesis of Anaemia in Sepsis.** (О патогенезе анемий при гнойно-септических процессов) A. I. Krakovskiĭ. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **34**, 34–40, No. 10, Oct., 1956. 23 refs.

In an attempt to elucidate the mechanism of the development of anaemia in patients suffering from sepsis the author has studied the erythropoietic function of the bone marrow in 102 patients; in the course of the investigation 160 sternal punctures and 284 blood analyses were carried out.

From the results of this study the following conclusions are drawn. (1) The anaemia most often develops in cases of chronic sepsis. The main factor in the pathogenesis is the slowing down of the second step in erythropoiesis, namely, the maturing of the erythroblasts. This is thought to result from a breakdown in the circulation of iron, the iron being utilized in the reticulo-endothelial system for the immuno-biological processes of resistance to infection, as well as being fixed in the septic foci. In addition, the slowing down of gastric secretion which occurs in generalized sepsis prevents absorption of exogenous iron. Thus the production of haemoglobin is slowed down, this leading to the appearance of oligochromic erythrocytes and anaemia. (2) The occurrence of massive haemolysis in the anaemia of sepsis is rare, but some degree of haemolysis may sometimes aggravate the anaemia. (3) Since no evidence was found of any suppression of the first stage of erythropoiesis in sepsis it is concluded that the process of primary erythroblastosis is not affected. (4) Likewise there was no evidence of suppression of erythropoiesis as a result of an increase in granulopoiesis, that is, production of the high leucocytosis consequent on infection.

A. Koby

1059. **Studies of the Anemia and Iron Metabolism in Cancer**

A. Miller, R. B. Chodos, C P. Emerson, and J. F. Ross. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 1248–1262, Nov., 1956. 12 figs., 40 refs.

The authors have studied iron metabolism in the anaemia associated with neoplastic disease at the Massachusetts Memorial and Boston Veterans Administration Hospitals. The erythrocyte volume was determined in some of the 38 cases of carcinoma studied by the radioactive-phosphorus method and in others by the azovan-blue dye technique. The survival of the patients' own erythrocytes labelled with radioactive chromium was determined and the turnover of radioactive iron (^{59}Fe) was estimated from the disappearance from the plasma of the intravenously administered isotope.

It was found that hypoferraemia with normal quantities of storage iron sometimes occurred in patients with cancer, the fall in the serum iron concentration being correlated with dissemination of the tumour growth. The storage iron, determined by examining post-mortem sections of liver and spleen, was normal. Erythrocyte survival studies revealed evidence of erythrocyte destruction in 7 out of 12 patients. The rate of erythrocyte production was normal or increased in 29 (out of 38) patients in this series, and the authors suggest that there is a " functional inadequacy " of erythropoiesis in the anaemia of neoplastic disease. The depression of the serum iron level was associated with a more rapid disappearance of the intravenously injected ^{59}Fe.

I. McLean Baird

1060. **Portal Fibrosis in Acute Leukaemia**

G. Wetherley-Mein and D. G. Cottom. *British Journal of Haematology* [*Brit. J. Haemat.*] **2**, 345–354, Oct., 1956. 6 figs., 5 refs.

The presence of considerable portal fibrosis is described in a child suffering from acute leukaemia who was treated with folic-acid antagonists. The changes in the portal tracts of 21 patients with acute leukaemia are reviewed and discussed. These patients had received various forms of treatment, including folic-acid antagonists. A number of them showed varying degrees of portal fibrosis. The development of portal fibrosis could not be related to age, type of leukaemia, duration of disease, type of treatment or satisfactory response to treatment. The histological changes observed suggested that portal fibrosis in acute leukaemia is probably of the same order as the marrow fibrosis observed in the myelofibrosis–leukaemia syndrome.—[Authors' summary.]

1061. **Prednisone Therapy of Acute Lymphatic Leukemia in Children**

C. B. Hyman and P. Sturgeon. *Cancer* [*Cancer* (*Philad.*)] **9**, 965–970, Sept.–Oct., 1956. 12 refs.

In a therapeutic trial of prednisone in the treatment of acute lymphatic leukaemia in children, here described from the Los Angeles Children's Hospital, California, 21 children aged 5 months to 10 years were given a total of 27 courses of therapy; the illness had lasted for periods ranging from 14 to 300 days and 8 of the patients had had no previous therapy. A dose of 0·66 to 1·0 mg. of prednisone per lb. (1·45 to 2·2 mg. per kg.) body weight per day was given initially and 1·5 mg. per lb. (3·3 mg. per kg.) per day in second courses. In order to facilitate comparison of the results with those of other workers the " Criteria for Evaluation of Response to Therapy of Acute Leukaemia " of the U.S. Cancer Chemotherapy National Service Center were used in analysing the findings.

After the 27 courses complete remissions were recorded in 6 instances (in 5 of which prednisone was the first form of therapy used), partial remission in 12, clinical remission in 8, and no response in one. The remissions lasted from 19 to 107 (mean 57) days. The period of

remission after second courses was shorter, and although the degree of remission, as judged by the criteria used, might be similar, the bone marrow frequently showed less regression of primitive cells. Nevertheless these remissions compared favourably with those obtained with cortisone and ACTH, as reported in the literature.

Mary D. Smith

1062. **Treatment of Chronic Myeloid Leukaemia with Mercaptopurine**

J. R. FOUNTAIN. *British Medical Journal* [*Brit. med. J.*] **2**, 1345–1348, Dec. 8, 1956. 6 refs.

The author, from the General Infirmary at Leeds, reports his experience of 6-mercaptopurine in the treatment of 15 patients suffering from chronic myeloid leukaemia. The drug was given in a dosage of 150 to 200 mg. daily, this being reduced as the leucocyte count fell to normal until an optimum maintenance dose of 50 to 150 mg. daily was reached. Regression of clinical evidence of the disease was observed in all 15 patients, and in 11 of them clinical improvement, except for slight enlargement of the spleen in some, was considered to be complete. Remission lasting up to 2½ years was observed, the patients being able to resume their normal activities.

There was a delay in response to treatment of 1 to 3 weeks, after which the leucocyte count fell rapidly. When treatment ceased the leucocyte count continued to fall for a period, but if a maintenance dose was not given relapse was likely to occur within a month of stopping treatment. In 12 patients definite improvement in erythropoiesis and haemoglobin synthesis followed treatment. The author states that with this dosage scheme serious thrombocytopenia was not observed, but that the blood picture should be checked at regular intervals.

I. M. Rollo

1063. **Treatment of Hodgkin's Granuloma, Chronic Lymphatic Leukaemia, Polycythaemia Vera, and Other Reticuloses with Triethylenethiophosphoramide**

B. J. LEONARD, M. C. G. ISRAËLS, and J. F. WILKINSON. *Lancet* [*Lancet*] **2**, 1017–1021, Nov. 17, 1956. 1 fig., 10 refs.

The authors, in this paper from the University and Royal Infirmary, Manchester, report their experience with triethylenethiophosphoramide (thio-TEPA) in the treatment of 52 patients suffering from polycythaemia vera, chronic lymphatic leukaemia, lymphoid reticulosis, follicular lymphoreticulosis, Hodgkin's granuloma, reticulum-cell reticulosis, and reticulosarcoma. The drug was given intramuscularly in normal saline in a dosage of 25 mg. on the first day, followed by 25 to 50 mg. on alternate days, treatment being controlled by the blood count.

In 14 cases of polycythaemia vera the results were excellent, remission lasting from 7 to 14 months being achieved and a second course of the drug producing a further remission. Thio-TEPA was also effective in cases of Hodgkin's granuloma, lymphoid reticulosis, and follicular reticulosis when the disease was mainly detectable in peripheral lymph nodes. The authors emphasize that the drug should not be given when the platelet count is low. Side-effects, which were observed in about half the cases, included anorexia, nausea, and vomiting.

G. Calcutt

1064. **Dangerous Contaminants in Stored Blood**

M. G. MCENTEGART. *Lancet* [*Lancet*] **2**, 909–911, Nov. 3, 1956. 2 figs., 12 refs.

It has been shown that certain Gram-negative bacilli can grow in stored blood at refrigerator temperature and may reach a high concentration, thus causing a fatal shock-like syndrome if the blood is used for transfusion, even in amounts as small as 20 ml.

In this paper from the University of Aberdeen the author describes 2 cases in which transfusion with stored blood contaminated with a *Klebsiella*-like organism proved fatal. In the first case a rigor occurred after the transfusion of only 20 ml. of stored blood; the transfusion was stopped immediately, but the patient developed acute circulatory failure and died 2 hours later. In the second case the patient died within 12 hours of transfusion of 50 ml. of similar blood but from a different bottle. In both cases the blood was of permanganate colour but there was no obvious haemolysis. The same organism was recovered from both bottles and resembled, but was not identical with, *Klebsiella cloacae*; the organism, which is described, grew well at temperatures of 4° to 30° C., but showed no growth at 37° C. The author suggests that any blood to be used for transfusion in or after the third week of storage should be examined by means of a stained film to exclude the presence of bacteria.

Kate Maunsell

1065. **Ammonia Levels in Transfused Blood**

P. W. SPEAR, M. SASS, and J. J. CINCOTTI. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **48**, 702–707, Nov., 1956. 1 fig., 18 refs.

In view of the suggestion that exogenous protein and other nitrogenous substances, including ammonia, may in certain circumstances be related to the syndrome of hepatic coma the authors, at the Veterans Administration Hospital, Brooklyn, New York, have determined the ammonia content of bank blood which had been stored for varying periods at 4° C.

Values for ammonia level ranged from 128 to 930 μg. per 100 ml., the higher values being as a rule found in blood stored for 20 or more days. Serial determinations showed that the ammonia content of the stored blood increased linearly with time, at least up to 15 days, after which it gradually declined. The addition of 5 ml. of 20% sodium glutamate to 250 ml. stored blood resulted in a decrease of about 22% in the rate of ammonia formation as compared with a duplicate control sample of blood to which no glutamate was added. Further tests showed that the high ammonia content of bank blood is due to preformed ammonia and not to the glutamine normally present in blood. It is pointed out that the ammonia content of bank blood may be of clinical importance, particularly if aged blood is used for the transfusion of patients on the verge of hepatic insufficiency.

M. Lubran

Respiratory System

1066. **Needle Biopsy of the Parietal Pleura**
P. HELLER, W. F. KELLOW, and B. CHOMET. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 684–690, Oct. 11, 1956. 5 figs., 15 refs.

At the Veterans Administration Hospital (University of Illinois), Chicago, 20 patients were subjected to pleural biopsy with a Vim–Silverman needle, a pleural effusion being the clinical indication in each case. The procedure was found to be useful as a rapid method of confirming, or in a few cases as providing the first clue to, the cause of the effusion. Of particular interest was the finding of tuberculous granulation tissue in the parietal pleura in 5 cases. No serious complications were encountered.
P. Mestitz

LUNGS AND BRONCHI

1067. **Further Experiences with the Method of Controlled Unilateral Pulmonary Artery Occlusion in the Study of Lung Function**
P. NEMIR, H. H. STONE, H. R. HAWTHORNE, and T. N. MACKRELL. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **32**, 562–575, Nov., 1956. 8 figs., 5 refs.

In this paper from the University of Pennsylvania the authors report the results in 35 patients of unilateral occlusion of the pulmonary artery for 20 to 60 minutes by inflation of a balloon on the end of a triple-lumen cardiac catheter. This procedure of "medical pneumonectomy" has been used by various groups of workers to assess the likely effects of subsequent operation in almost 300 patients without mortality. In the present series bronchospirometry with main-bronchus occlusion was not carried out concurrently. In 5 of the 35 patients it was impossible to position the balloon satisfactorily. Complications included some ventricular extrasystoles during positioning of the catheter and a transient rise in temperature about 3 hours after the procedure was completed. Using 2 of the 3 lumina, the authors were able to record blood pressure and obtain blood samples for gas analysis both proximal and distal to the occluding balloon, the third lumen being used for inflation of the balloon at will.

There was always a very poor outcome, with respiratory insufficiency, from subsequent operation in those cases showing increase in the resting pulmonary arterial pressure with a sustained rise following the temporary occlusion. Even if the resting pressure was not raised, a sustained increase following occlusion nearly always indicated a poor prognosis. The results of blood gas analyses were not very informative, but the distal blood pressure after inflation of the balloon was found to be as reliable as the wedge capillary pressure determined by conventional catheterization.

It would appear from these findings that lung resection is contraindicated in patients without malignant disease showing a sustained pressure after temporary occlusion of the pulmonary artery. The authors add that even in the presence of malignant disease lobectomy is to be preferred to pneumonectomy. The investigative procedure described, although "difficult and arduous . . . and certainly not applicable for use as a routine", is considered to be of value when there is doubt about the advisability of lung resection. *P. Hugh-Jones*

1068. **Friedländer Bacillus Infection of the Lung. With Special Reference to Classification and Pathogenesis**
L. D. ERASMUS. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 507–521, Oct., 1956. 6 figs., 43 refs.

During the 3-year period 1952–4, 17 cases of Friedländer bacillus infection of the lung were seen at the Pretoria General Hospital, South Africa. In 14 of these the bacillus was considered to be the primary invader, a primary infection being diagnosed if the specific organism was isolated from the sputum in pure culture or as the predominant organism on at least two successive days. The author suggests the following classification of Friedländer bacillus infections: (1) primary, (*a*) acute, and (*b*) chronic (abscess formation); (2) secondary, (*a*) associated with other organisms in various forms of bacterial pneumonia, and (*b*) associated with other organisms in various other pathological lung conditions, such as asthma, bronchitis, bronchiectasis, cystic disease, and neoplasms.

Of the 14 patients with primary infection 11 were males (9 Bantus and 2 Europeans) and 3 were females (2 Bantus and 1 European), and their ages ranged from 16 to 76 years. The first 6 primary infections occurred among 260 cases of pneumonia. The incidence of the infection was highest in the summer, when 11 of the 17 cases were diagnosed.

In primary infections the onset was sudden, with fever, pleuritic chest pain, and cough with blood-stained or purulent sputum which varied in amount from ½ to 12 oz. (14 to 340 ml.) daily and resembled in most cases the sputum of ordinary suppurative pneumonia. In about half of the cases there was a previous history of chest infection (cough, hoarseness, and sore throat). Clinical signs of segmental and bronchopneumonic consolidation were present in all cases. The leucocyte count varied from 4,000 to 25,900 per c.mm. (polymorphonuclear leucocytes from 69 to 84%). Radiological examination of the chest showed that the lesion was unilateral in the right lung in 9 of the cases of primary infection and bilateral in the remaining 5. In 7 of the unilateral cases the lesion was confined to the posterior segment of the upper lobe.

The treatment regimen in the present series included: 500,000 units of penicillin intramuscularly twice daily; an initial dose of 2 g. of sulphadiazine followed by 1 g. 4-hourly; 0·5 g. of streptomycin intramuscularly every

6 hours for 2 days followed by 0·5 g. twice daily; chloramphenicol, chlortetracycline (aureomycin), and oxytetracycline 1 g. initially by mouth followed by 0·5 g. 6-hourly. Sensitivity tests *in vitro* showed that the organism was highly sensitive to streptomycin in all cases, to chloramphenicol in 13, to sulphadiazine in 8, to oxytetracycline in 6, and to chlortetracycline in 3. In all cases the organism was uniformly resistant to penicillin, erythromycin, tetracycline, and carbomycin.

There were no fulminating cases and no deaths in the series. Of the 17 patients, 8 were fit and well in 3 weeks. Cavitation occurred in 7 cases, surgical resection being performed on this account in 2. Lobectomy specimens (2 cases) showed thick dense pleura, and the underlying lung was seen to be fibrotic, with areas of consolidation, collapse, and abscess formation, the walls of the abscesses being ragged and thick.

The author concludes that the radiological findings and the presence of gross dental sepsis, which was the most frequently observed form of upper respiratory tract infection, indicate that the disease is an aspiration pneumonia caused by the inhalation during sleep of the Friedländer bacilli normally present in the teeth, mouth, and upper respiratory tract. *I. M. Librach*

1069. **The Mediastino-cardiac Syndrome in Cancer of the Lung and in Leucosis.** (Медиастино-кардинальный синдром при раке легкого и лейкозе)
V. S. Nesterov. *Терапевтический Архив* [*Ter. Arkh.*] **28**, 3–10, No. 7, 1956. 2 figs., 6 refs.

Discussing the view that metastatic cancer of the heart presents very few characteristic signs the author notes that some previous workers have regarded the absence of such signs as of clinical significance, while others have spoken of the striking insusceptibility of the heart muscle to malignant growths, or have pointed out that such cases cannot be differentiated from ordinary cardiac insufficiency.

The syndrome of cancerous involvement of the heart, here described from the Voronezh Medical Institute, is based on a detailed study of 8 cases of pulmonary cancer with involvement of the heart (7 by extension and 1 by metastasis). The nine main elements of the syndrome are as follows. (1) Pressure on other mediastinal organs. (2) Pressure on the superior vena cava. (3) Retrograde collateral venous flow in the anterior abdominal wall (or chest wall in the case of pulmonary cancer) from the territory of the superior to that of the inferior vena cava. (4) Pressure on the aorta or pulmonary artery by the cancerous growth or in the anterior and posterior mediastina by leucotic tumours of lymph nodes. (5) increased blood pressure in children and adolescents as a result of pressure on the aorta. (6) A coarse systolic murmur over the aorta, conducted to the interscapular region, and over the pulmonary artery. (7) Disturbances of conduction and the development of arrhythmia and of cardiac insufficiency (in the absence of other causes for their appearance). (8) Clinical and radiological signs of pericarditis. (9) Failure of the usual methods of treatment of the apparent cardiac condition.
R. Crawford

1070. **Valsalva's Manœuvre in Healthy and Emphysematous Subjects.** (Valsalvaversuch bei Gesunden und Emphysemkranken)
E. Lüthy. *Archiv für Kreislaufforschung* [*Arch. Kreisl-Forsch.*] **24**, 260–273, Oct., 1956. 5 figs., 34 refs.

During an investigation at the University Medical Clinic, Berne, into " cough syncope " the author observed that this phenomenon was confined almost entirely to patients with emphysema, and so was led to an investigation of the circulatory changes during Valsalva's manœuvre in 25 such patients, whose response to the manœuvre was compared with that of 28 healthy subjects.

Normally, as a result of increased intrathoracic and intra-abdominal pressure, there is an immediate rise in the blood pressure at the beginning of the manœuvre, the systolic pressure being affected more than the diastolic. Subsequently there is a slow fall in blood pressure over an average period of 6 seconds, after which the pressure rises once more and may exceed the original values. At the end of the manœuvre both the systolic and diastolic pressures fall rapidly, this being followed by a rapid rise which exceeds resting values. Finally, there is a gradual fall to the original levels. In patients with emphysema the initial fall in blood pressure is more marked than in the normal subject, the lowest values being recorded after an average period of 9 seconds, and there is also a marked diminution in pulse pressure. Frequently the blood pressure fails to rise at this point, and in some cases may continue to fall after termination of the manœuvre to a level likely to cause syncope; subsequently there is often an " overshoot " which is more marked than in normal subjects. The initial fall in blood pressure exceeds that observed in the normal subject, even when the latter is exerting a maximum expiratory effort.

In view of these findings the author concludes that there is a fundamental difference in the mechanism of Valsalva's manœuvre in normal and emphysematous subjects. In the former the impediment to venous return and the consequent cardiac filling are important factors. Experiments involving the injection of contrast media showed almost complete cessation of the blood flow through the vena cava during Valsalva's manœuvre, a surprising finding in view of the increase in intra-abdominal pressure at that time; further, the author has shown that the increase in abdominal pressure is not communicated to the right auricle. He concludes that there is mechanical obstruction of the inferior vena cava as a result of its compression by the diaphragm, and that this is more marked in people with emphysema than in normal subjects. He further postulates that a similar mechanism may cause " pseudo right heart insufficiency " during effort. *F. Starer*

1071. **Effects of Venesection on Pulmonary and Cardiac Function in Patients with Chronic Pulmonary Emphysema and Secondary Polycythemia**
J. H. Auchincloss and J. J. Duggan. *American Journal of Medicine* [*Amer. J. Med.*] **22**, 74–82, Jan., 1957. 21 refs.

Endocrinology

1072. **A Comparison of the Effects of Acetylsalicylic Acid and DL-Triiodothyronine in Patients with Myxoedema**
W. D. ALEXANDER and K. W. M. JOHNSON. *Clinical Science* [*Clin. Sci.*] **15**, 593–601, Nov., 1956. 3 figs., 18 refs.

On the basis of the finding that salicylate increases the metabolic rate in man the authors have compared the effects of administration of aspirin and DL-3:5:3′-triiodothyronine on clinical features and laboratory findings in 4 myxoedematous patients (3 females and one male) at the Western Infirmary, Glasgow. After a control period aspirin was given for 16 days in a maximum daily dose of 8·1 g.

During the period of aspirin administration the patients became subjectively and objectively warmer and their appetites improved, but there were no other changes in their clinical state. The basal metabolic rate (B.M.R.) increased by 28% to 36%, blood cholesterol level fell, circulation time diminished, but the electrocardiogram remained unchanged. Administration of triiodothyronine had a quantitatively similar effect on the B.M.R., but in addition it also relieved other clinical manifestations of myxoedema. In 2 patients suffering from angina pectoris an increase in the B.M.R. and cardiac output due to aspirin did not aggravate the incidence of the pain; but in the same patients similar increases in B.M.R. brought on by triiodothyronine markedly increased the severity of the angina.

It is the authors' impression that aspirin might be useful to supplement thyroid extract in the treatment of myxoedematous patients in whom the occurrence of anginal pain precludes adequate thyroid medication.

Marcel Malden

ADRENAL GLANDS

1073. **Clinical and Metabolic Effects of Δ^1-Dehydro-9-alpha-fluoro-hydrocortisone Acetate**
L. VILLA, G. SALA, and C. B. BALLABIO. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 237–240, Sept., 1956. 3 figs., 17 refs.

The authors carried out a clinical trial of a new derivative of hydrocortisone, Δ^1-dehydro-9-α-fluorohydrocortisone acetate, at the University of Milan in 3 cases of rheumatoid arthritis, one of chronic gout, and 2 of Addison's disease. In the 4 cases of rheumatic affections the drug was given by mouth in a daily dose of 4 to 10 mg. for 10 days, while in the 2 cases of Addison's disease 0·5 to 1 mg. daily was given for a 7-day period.

In all cases antirheumatic activity was marked, with subjective and objective improvement taking place within 48 hours of the start of therapy. In the case of gout there was both local and general improvement. Withdrawal of the drug was followed by relapse. The metabolic effects of Δ^1-dehydro-9-α-fluorohydrocortisone acetate were even more marked, leading to marked decrease in the serum potassium level to 2 to 2·5 mEq. per litre, slight increase in serum sodium concentration, and water retention, causing increase in weight. This was accompanied by a rise in blood pressure, increase in heart size, and decrease in heart rate, with abnormalities in the electrocardiogram consisting in lengthening of the Q–T interval, displacement of the ST segment, and depression of the T wave. In one of the patients with rheumatoid arthritis the drug produced frank diabetes, but no effect on glucose tolerance was noted in the other cases. In the 2 cases of Addison's disease electrolyte metabolism returned to normal limits with the small doses used.

These results are interpreted as showing that Δ^1-dehydro-9-α-fluorohydrocortisone acetate is 10 to 25 times more potent than cortisone acetate, but that its use in rheumatic affections is precluded by its marked effect on electrolyte metabolism. It is suggested that it may, however, be useful in the treatment of adrenal insufficiency.

H. F. Reichenfeld

1074. **The Excretion of 17-Ketosteroids in the Urine of Patients with Generalised Carcinomatosis Secondary to Carcinoma of the Breast**
B. J. ALLEN, J. L. HAYWARD, and W. H. H. MERIVALE. *Lancet* [*Lancet*] **1**, 496–499, March 9, 1957. 9 figs., 22 refs.

1075. **Primary Aldosteronism**
M. D. MILNE and R. C. MUEHRCKE. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **49**, 883–885, Nov., 1956. 2 figs., 10 refs.

Increased production of aldosterone, the natural mineralocorticoid of the adrenal cortex which has a profound influence on sodium and potassium metabolism, may be of 3 types: (1) physiological, from sudden reduction of the blood volume, as in severe haemorrhage; (2) secondary, occurring in clinical states associated with severe oedema, such as the nephrotic syndrome; and (3) primary. The first case of primary aldosteronism was described by Conn in 1955, and since then 3 other cases have been published in detail. The present authors now report 2 more cases seen at Hammersmith Hospital (Postgraduate Medical School of London) in the last year.

The clinical findings in these 6 cases (3 of them in coloured patients) are summarized. All have shown potassium depletion with excessive urinary potassium loss, associated with comparatively mild hypertension, and characteristic abnormalities of the plasma electrolytes, sodium and bicarbonate levels being increased and potassium and chloride levels reduced. In all but one

of the cases (the authors' second case) there were attacks of hypokalaemic muscular weakness or paralysis. In the one male patient the condition was due to adrenal cortical carcinoma and in the 5 female patients to adrenal cortical adenoma.

The authors' first patient was a coloured woman aged 43 years who had a 12-year history of attacks of prolonged hypokalaemic muscular paralysis. Balance studies showed a deficiency of 1,000 mEq. of potassium —about one-third of the normal body content. Removal of the adrenal cortical adenoma was followed by a reduction in blood pressure and relief of hypertensive cardiac failure, while the plasma electrolyte levels returned to normal values. Their second patient, a woman aged 58, is the only case of asymptomatic primary aldosteronism yet described, the patient's only complaint being of mild occipital headache. Routine examination showed some hypertension and slight left ventricular enlargement. Electrocardiography suggested that there might be potassium depletion, and biochemical studies revealed a deficiency of 400 mEq. of potassium. Although perirenal air insufflation with tomography failed to show any adrenal tumour and the urinary excretion of aldosterone was normal, surgical exploration was nevertheless undertaken by the anterior abdominal approach to allow of examination of both adrenal glands. The left adrenal gland, which contained a small encapsulated adenoma, was removed; the blood pressure has since returned to normal and the biochemical abnormalities have disappeared.

The authors suggest that probably all cases are at first like their second case. At this stage the condition can be recognized only by means of electrocardiography and biochemical investigation of all cases of benign hypertension. As potassium depletion increases, symptoms of muscular weakness or paralysis appear and later, if treatment is delayed, there is a grave risk of irreversible renal damage *Kenneth Stone*

1076. **The Effect of Changes in Body Sodium on Extracellular Fluid Volume and Aldosterone and Sodium Excretion by Normal and Edematous Men**

L. E. DUNCAN, G. W. LIDDLE, and F. C. BARTTER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 1299–1305, Nov., 1956. 5 figs., 27 refs.

A study is reported of the metabolic response to intravenous administration of saline in 2 healthy subjects, 2 patients with portal cirrhosis, and 5 patients with congestive heart failure. The sodium and potassium content of the diet, urine, faeces, and blood, and the urinary excretion of 17-hydroxycorticoids and of aldosterone were estimated, the last-named by bioassay in adrenalectomized dogs. In order to induce sodium depletion each subject ingested daily 43 g. of a carboxylic exchange resin in the hydrogen and potassium form, and was then given intravenously 2 litres of saline containing 253 millimols of sodium chloride and 55 millimols of sodium lactate.

The metabolic response of the healthy subjects and the patients was qualitatively the same. The pattern was: (1) increase in weight, suggesting expansion of the extracellular fluid as a result of the intravenous saline infusion; (2) decrease in the urinary concentration of aldosterone; (3) rise in the urinary excretion of sodium; and (4) rise in the sodium uptake by the resin in the faeces. This suggests that an increase in the body content of sodium results in a decrease in the circulating aldosterone, as estimated from the urinary excretion of the hormone. In the patients with cirrhosis and in 4 of the 5 patients with heart failure the urinary excretion of sodium did not increase to such a high level and the circulating aldosterone did not fall to such a low level as in the healthy subjects. The authors suggest that this reduced metabolic response may contribute to the occurrence of oedema in patients with heart failure and portal cirrhosis.

I. McLean Baird

1077. **The Regulation of Aldosterone Secretion in Man: the Role of Fluid Volume**

F. C. BARTTER, G. W. LIDDLE, L. E. DUNCAN, J. K. BARBER, and C. DELEA. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 1306–1315, Nov., 1956. 10 figs., 29 refs.

The part played by fluid volume in the control of aldosterone secretion was studied in 18 healthy controls, one patient with diabetes insipidus, and one patient with panhypopituitarism, who were maintained in strict metabolic balance. Sodium deprivation resulted in loss of weight, decrease in urinary excretion of sodium, and an increase in urinary excretion of aldosterone. These changes occurred within 24 hours if mercurial diuretics were given and were observed in the patient with panhypopituitarism and in 4 controls. Expansion of body fluids by administration of vasopressin tannate in oil and additional water resulted in gain in weight, a fall in the serum concentration of sodium, and a decrease in urinary excretion of aldosterone.

A further experiment was carried out to determine the effect of contraction of body fluids without sodium depletion. In 5 healthy subjects and the 2 patients with pituitary dysfunction, dehydration concurrently with administration of a diet containing moderate amounts of sodium caused a decrease in fluid volume and an increase in the serum sodium concentration and osmolarity. There followed diuresis, loss of weight, a rise in the serum sodium level, and an increase in the urinary excretion of aldosterone.

In 4 sodium-depleted subjects expansion of the extracellular fluid volume was achieved by giving hypertonic saline intravenously, the effect again being contraction of the intracellular fluid volume, while in each case there was a fall in urinary aldosterone excretion. Finally the effect of simple dehydration was compared with that of "extracellular dehydration" produced by mercurial diuretics; no change was observed in the serum sodium concentration. It was apparent that changes in total body water were less effective in influencing aldosterone excretion than much smaller changes in extracellular fluid volume.

The authors discuss the mechanism of aldosterone regulation in relation to the experimental results.

I. McLean Baird

DIABETES

1078. **Hypophysectomy for Diabetic Retinopathy. A Preliminary Report**
R. A. SCHIMEK. *A.M.A. Archives of Ophthalmology* [*A.M.A. Arch. Ophthal.*] **56**, 416–425, Sept., 1956. 39 refs.

In this paper from the Henry Ford Hospital, Detroit, the author reviews the evidence in favour of removal of the pituitary gland in severe diabetes, and notes that in diabetic patients subjected to hypophysectomy the reported early postoperative mortality ranges from 3 to 10%.

He then describes 5 cases in which hypophysectomy was performed without mortality. In 4 of the patients with severe retinopathy there was a marked tendency after operation for the haemorrhages to clear (although one relapse occurred). The exudate and retinitis proliferans were unaffected. In the remaining patient with less severe retinopathy considerable improvement in vision was noted. *R. Smith*

1079. **Diabetic Retinopathy: Lack of Correlation with Vitamin B_{12} Excretion**
J. J. BOOKMAN, R. H. JOELSON, W. G. TOLL, H. BAKER, and H. DOLGER. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **5**, 26–28, Jan.–Feb., 1957. 3 figs., 10 refs.

1080. **Contemporary Problems of Metabolism in Diabetes and Obesity.** (Современные вопросы патологии обмена веществ при диабете и ожирении)
S. M. LEITES. *Советская Медицина* [*Sovetsk. Med.*] 38–44, No. 9, Sept., 1956.

Hyperglycaemia has been regarded as being due to decreased synthesis of glycogen in the liver and to diminished utilization of sugar by the tissues. But in experimental alloxan diabetes the level of glycogen in the liver and muscles is normal or even raised, and liver biopsy has revealed a similar finding in clinical diabetes. Bertram and Dove have suggested that some forms of diabetes are due to increased breakdown of glycogen due to imbalance between the α and β cells in the pancreatic islets, while Ferner holds that the hypophysis stimulates the α cells and that pituitary diabetes is caused by excessive production of the α-cell hormone glucagon. There is, however, insufficient experimental evidence to estimate the real importance of the α cells and of glucagon in chronic diabetes.

The chief cause of hyperglycaemia in diabetes is probably a defect in the conversion of carbohydrate into fat. In addition, there is diminished activity of glucokinase, which lowers the rate of phosphorylization of glucose and hence the utilization of it by the tissue cells, and likewise affects the synthesis of fat and protein which accompanies glucose oxidation. The glycosuria in diabetes is a consequence of increased filtration of glucose during hyperglycaemia, combined with the diminished reabsorption by the tubules caused by the diminished phosphorylization. So-called renal glycosuria differs from pancreatic diabetic glycosuria in that, while in both cases phosphorylization is defective, in renal glycosuria this is the sole defect, whereas in diabetes other metabolic defects are present, including a diminished power of synthesizing amino-acids.

Ketosis is due to (1) a reduction in the synthesis of the higher fatty acids from aceto-acetic acid, and (2) disturbance of the so-called tricarbon oxidation cycle, in which the reaction of aceto-acetic and acetic acid with co-enzyme A results in the oxidation of oxalo-acetic acid to carbon dioxide and water, citric acid being formed during the process. Ketosis is not directly connected with insulin deficiency, but with fatty infiltration of the liver. It is severe in only one-third of patients with diabetes, and in these cases, therefore, there must be additional factors which conduce to ketosis, such as deficiency of lipocaic or increase in the output of growth hormone by the pituitary or in the output of adrenocortical hormones. Ketone bodies are formed as a result not only of imperfect fat metabolism, but also of defective protein metabolism in which there is production of such ketogenic amino-acids as phenylalanine, tyrosine, or leucine. Hence the need in treating diabetes for the inclusion in the diet of lipotrophic substances such as choline, methionine, and foods rich in casein, ascorbic acid, folic acid, and cyanocobalamin.

Obesity not associated with over-eating is thought to be due to excessive activity of the cells in the fat depots, which have a greater capacity for converting glucose into fat than the cells of the liver. The metabolic function is under control of the central nervous system, sympathetic impulses inhibiting the process of conversion, while parasympathetic action reinforces it. The administration of insulin can increase the conversion rate tenfold according to Hausberger, while pituitary growth hormone has the opposite effect. In the hereditary and hypothalamic forms of obesity there is often an absolute or relative increase in function of the pancreatic islets, which is shown by an increased tolerance of glucose, followed at a later stage by lowered tolerance and hyperglycaemia. The alimentary centre postulated by Pavlov as functionally uniting the nervous impulses in the cortex, subcortex, and hypothalamus plays an important role in the type of obesity associated with increased appetite and over-eating. But in this "exogenous" form of obesity too the same metabolic factors come into play, and Mayer has shown that there is increased conversion of carbohydrate into fat and a diminished loss of fat from the depots. It is therefore difficult to distinguish pathologically between endogenous and exogenous adiposity.

The aim in the treatment of obesity should be to lower the rate of lipogenesis. Hausberger has shown experimentally that this can be achieved by a diet low in carbohydrates and rich in fats, and, while Penington's diet (1 to 2% carbohydrate, 80% fat, and 18% protein) is far from physiological and liable to cause ketosis, a modification of it in which carbohydrates are limited to 150 to 200 g. per day, with a full normal fat ration, is valuable. A uniformly spaced and frequent ingestion of food in the 24 hours produces less lipogenesis than the same amount given in one or two meals. Physiotherapy and massage stimulate metabolism and are

valuable in obesity; sympathomimetic drugs diminish lipogenesis, but have unpleasant and dangerous side-effects. Further research is needed to find chemical and hormonal preparations which will control lipogenesis without producing these undesirable manifestations of general sympathetic stimulation.

L. Firman-Edwards

1081. **Diabetes and Altered Carbohydrate Metabolism in Patients with Cancer**

A. S. GLICKSMAN and R. W. RAWSON. *Cancer* [*Cancer (Philad.)*] **9**, 1127–1134, Nov.–Dec., 1956. 5 figs., 45 refs.

1082. **The Oral Antidiabetic Compounds: Selection of Patients by Means of a Blood Sugar Response Test. Preliminary Report**

C. WELLER. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **56**, 3333–3337, Nov. 1, 1956. 9 refs.

This is a preliminary report from Grasslands Hospital, Valhalla, New York, on the indications and use of carbutamide (1-butyl-3-*p*-aminobenzenesulphonylurea) and tolbutamide (1-butyl-3-*p*-tolylsulphonylurea) in diabetes mellitus. A simple test for selecting patients for treatment with these drugs is described. The fasting blood sugar level is estimated on the morning of the test and the patients are given by mouth 3 g. of either carbutamide or tolbutamide. Another blood sugar determination is made 3 to 6 hours later with the patient still fasting. If there is a 20% reduction in blood sugar level the patient is considered to have responded successfully to the treatment.

A. I. Suchett-Kaye

1083. **Studies on Humoral Insulin Antagonists in Diabetic Acidosis**

J. B. FIELD and DEW. STETTEN. *Diabetes* [*Diabetes*] **5**, 391–395, Sept.–Oct., 1956. 14 refs.

A number of substances such as growth hormone and adrenocorticosteroids, which can be shown to have anti-insulin action *in vitro* and *in vivo*, have been suggested as factors in the causation and potentiation of human diabetes. With the development of methods of estimation of plasma insulin, attention has been directed to the possible occurrence and characterization of insulin antagonists in blood from diabetic patients. The chief difficulty is that the various assay methods assess only the effective insulin-like activity of the plasma—that is, the summation of the activities of insulin and any other insulin-like substances together with those of any antagonists present. It is therefore not surprising that the published literature is both conflicting and confusing.

The occurrence of immunological forms of insulin resistance associated with insulin inhibition by the gamma-globulin fraction of the plasma proteins has been reported (*J. Lab. clin. Med.*, 1956, **47**, 844), and the present authors, writing from the National Institutes of Health, Bethesda, Maryland, describe a different insulin antagonist present in patients who had never received insulin and could not, therefore, have developed antibodies to an exogenous product. The inhibitor was non-dialysable, migrated electrophoretically with the serum alpha-globulin fraction, was not a lipoprotein, and was devoid of insulinase activity. The presence of the antagonist in the blood of diabetic patients was associated with diabetic acidosis and disappeared after therapy with insulin. It was not associated with adrenal cortical hyperactivity or present in the serum of acromegalic diabetics.

M. J. H. Smith

1084. **Effect of Proteins on the Blood Glucose Levels**

G. JOACHIMOGLU and H. N. ANTONIADES. *Diabetes* [*Diabetes*] **5**, 383–387, Sept.–Oct., 1956. 13 refs.

The authors have studied the changes in blood glucose level after ingestion of various amounts of protein by healthy and diabetic human subjects at the Evangelismos Hospital, Athens. A total of 176 experiments were carried out on 80 healthy and 8 diabetic subjects, the materials tested including whole egg white, gelatin, and proteins isolated from lentil, oat, wheat, and pea-bean by salting-out procedures after a preliminary defatting. The proteins used were analysed for ash and nitrogen before and after digestion *in vitro* with pepsin, pancreatin, and diastase, the utilizable portion being calculated from the differences between the two sets of results. Each subject fasted for 12 hours and was then given a known amount of one of the proteins; blood glucose estimations (Hagedorn–Jensen) were made before, and at intervals of 3½ and 5 hours after, the administration. Any change of less than 10 mg. per 100 ml. in the blood glucose content was considered negligible.

The general conclusion derived from the study was that egg albumen had the highest rate of conversion to glucose, followed by oat protein, wheat protein, lentil protein, and pea-bean protein. Whereas 17 to 23 g. of egg white was enough to produce an increase of 10 to 30 mg. per 100 ml. in the blood glucose level of healthy subjects, 72 to 78 g. of pea-bean protein was necessary to produce the same effect. These amounts of proteins had no effect on the blood glucose levels of the diabetic subjects, and gelatin (30 g.) did not alter the blood sugar value of healthy subjects.

M. J. H. Smith

1085. **Compounds Inhibiting Insulin Degradation**

R. H. WILLIAMS and F. L. MARTIN. *Diabetes* [*Diabetes*] **5**, 451–456, Nov.–Dec., 1956. 13 refs.

Using an *in vitro* system consisting of a liver enzyme preparation which rapidly degrades insulin-^{131}I, it has been found that many different compounds inhibit the degradation of the hormone. Among the inhibitors are certain sulfonamides, disulfides, thiazoles and thioureas. Other types of sulfur compounds had a significant activity in the following order: phthalazinedithiol, sodium diethyldithiocarbamate, thiolhistidine, sodium heparinate, and decamethylenebisthiopseudourea. The most active nonsulfur compounds were, respectively: decamethylene-bisguanidine, indolepropionic acid, methylindole, arbutin, indole, phenylbutyramide, phenylpropionic acid and phenylacetic acid.

The mechanisms by which the compounds inhibit degradation and their effectiveness in lowering blood sugar are being investigated.—[Authors' summary].

The Rheumatic Diseases

1086. **Immunological Differentiation of Seral Antigens Specific to the Acute Phase of Rheumatic Processes.** [In English]
V. REJHOLEC and E. HALLER. *Acta rheumatologica Scandinavica* [*Acta rheum. scand.*] **2**, 145–160, 1956. 4 figs., 13 refs.

In the opinion of Wood *et al.* C-reactive protein is most likely a β globulin. It has also been shown that the basic component of the precipitate which forms when carbon dioxide is bubbled through diluted human serum is mainly β globulin. On the basis of these two facts the authors, working at the Research Institute of Rheumatic Diseases, Prague, passed carbon dioxide through diluted serum obtained from a patient in the acute stage of rheumatic fever. From the resulting precipitate an antiserum was prepared that was specific against precipitate-antigen. This was then absorbed on to collodion particles, and after incubation for 60 minutes at room temperature followed by centrifugation these were found to be agglutinated by the serum of patients with acute rheumatic fever, rheumatoid arthritis, myocardial infarction, and diffuse glomerulonephritis. The details of the preparation of the antiserum are described, together with procedures used to check its specificity against the antigen in the carbon dioxide precipitate. The results seem to confirm that this precipitate is chiefly β globulin with probably a small admixture of α and γ globulins, and from the clinical results it seems probable that it includes C-reactive protein.

In a clinical study the serum of more than 40 patients with rheumatic fever was tested with the antiserum. From the charts (reproduced) of 4 cases it can be seen that the results of this test followed closely the results for erythrocyte sedimentation rate (E.S.R.) by Westergren's method. The reaction was also found to precede a rise or fall in the E.S.R. by several days, or even to give a positive result when the E.S.R. was normal. In the fourth case treatment with cortisone appeared to deprive the test of its sensitivity. The test thus gives results very similar to the test for detection of C-reactive protein. The antiserum is claimed to be simpler to prepare than that for the detection of C-reactive protein, but since it loses its potency within 48 hours it must be freshly prepared, thereby making the test more complicated than the detection of C-reactive protein, for which commercial antisera are available. *G. H. Blair*

1087. **Therapeutic Trials in Acute Gouty Arthritis**
M. H. LEVIN, S. MARCUS, D. STRANGE, and R. L. SWEZEY. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 233–236, Sept., 1956. 17 refs.

In an attempt to elucidate the mode of action of some of the drugs known to have an effect on acute gouty arthritis, such as colchicine, ACTH (corticotrophin), cortisone, prednisone, and phenylbutazone, the authors have carried out, at the Veterans Administration Center, Los Angeles, a therapeutic trial on 15 patients with classic gout in which a number of drugs with a pharmacological action analogous to that of those mentioned above were tested.

(1) Three patients were treated with deoxycortone acetate, 10 mg. 12-hourly intramuscularly, because of the known sodium, chloride, and water retention produced by this hormone (an effect which it shares with the corticosteroids and which has also been demonstrated during colchicine therapy). In one patient the pain rapidly subsided, although there was no objective improvement in the affected joint; in the other 2 cases there was no apparent benefit. (2) In order to evaluate the local effect of colchicine 4 patients were given intra-articular injections of 1 mg. of colchicine (prepared as for intravenous use) into the affected joint; there was no improvement, but on the contrary 3 of the patients felt rather worse. (3) The administration of the antihistaminic diphenhydramine hydrochloride, 50 mg. 4-hourly intravenously, to 3 patients also proved ineffective, although no undesirable side-effects were noted. Finally, 5 patients were treated orally with doses of 1 mg. of colcemide (" demecolcine "), a drug differing from colchicine only in the substitution of a methyl group for the acetyl group of the latter; in these cases the response was good, being similar to that obtained with colchicine.

[This trial has thrown no further light on the mode of action of colchicine in acute gout.]

H. F. Reichenfeld

1088. **A Study of the Reactions of the Bone Marrow in Rheumatic Fever and Infections with Haemolytic Streptococci in Children.** (Etude des réactions de la moelle osseuse au cours du rhumatisme articulaire aigu et des infections à streptocoque hémolytique chez l'enfant)
M. BERNHEIM, C. MOURIQUAND, and D. GERMAIN. *Revue lyonnaise de médecine* [*Rev. lyon. Méd.*] **5**, 773–779, Oct. 30, 1956. 3 refs.

The authors have studied, at the Hôpital Edouard-Herriot, Lyons, the changes occurring in the bone marrow in 100 children with rheumatic fever at various stages of its evolution, and also in young patients with chorea (22 cases), scarlatina (16), acute nephritis (28), and other conditions (25). In order that the procedure should be as little upsetting to the child as possible they punctured a spinous process, or in some cases the anterior superior iliac spine, under local analgesia (2% lignocaine). Several films of the marrow were studied, analysis being made of not less than 1,000 cells.

The general conclusion was that the myelogram is of definite diagnostic value in atypical forms of rheumatic fever. The characteristic change was an increase in the number of plasmacytes; the average proportion of nucleated cells in the acute phase of rheumatic fever was 5·4% (range 2·3 to 15%), the normal value being taken as 0·4%. Lymphocytes also showed a definite

increase, but the proportions of neutrophil and eosinophil granulocytes were normal. In 33 cases a second myelogram was obtained some 2 to 4 weeks after the first, and a third myelogram in 11 of these, so that the effect of cortisone treatment could be observed. All the cases showed some reduction in the number of plasmacytes, but in the majority the figure did not fall to normal.

Similar changes were observed in the cases of chorea and scarlatina, and also in certain cases of acute nephritis in which there was evidence that a haemolytic streptococcus was concerned. A striking feature of the myelogram in scarlatina was an intense eosinophilia, as well as a marked plasmacytosis, clearly distinguishing it from rheumatic fever. *Kenneth Stone*

CHRONIC RHEUMATISM

1089. **Hydrocortisone *tertiary*-Butylacetate for Intra-articular Therapy in Rheumatic Diseases**

J. ZUCKNER, O. MACHEK, and A. M. AHERN. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 258–260, Sept., 1956. 4 refs.

Having noted that Hollander *et al.* (*J. Amer. med. Ass.*, 1955, **158**, 476; *Abstracts of World Medicine*, 1956, **19**, 62) obtained better results with hydrocortisone *tertiary*-butylacetate (T.B.A.) by intra-articular injection than with hydrocortisone acetate similarly administered, the authors, at the University School of Medicine, St. Louis, tried the intra-articular injection of the former in 18 patients with rheumatoid arthritis and 20 with osteoarthritis. An effort was made to maintain at least 50% decrease in pain and stiffness in the joint treated.

There was satisfactory benefit with hydrocortisone *tertiary*-butylacetate in about 80% of injected rheumatoid and osteoarthritic joints, the duration of improvement averaging 2 to 3 weeks. In 24 joints 2 or more injections each of hydrocortisone acetate and T.B.A. were given and the results compared. No significant difference between the effects of T.B.A. and hydrocortisone acetate could be demonstrated in 17 of the 24 joints. In most cases the knee-joint was injected and the dose of the acetate or of T.B.A. was 25 mg., although in a few instances 100 mg. was given. No advantage appeared to accrue from a dose of more than 25 mg. *C. E. Quin*

1090. **Use of Hypospray Jet Injector for the Intra-articular and Local Administration of Hydrocortisone Acetate**

M. ZIFF, V. CONTRERAS, and F. R. SCHMID. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 227–232, Sept., 1956. 3 figs., 6 refs.

In this paper from New York University College of Medicine, New York, the authors describe their experience with a hypospray jet injector for the intra-articular administration of therapeutically significant amounts of hydrocortisone acetate. This instrument (which was described in 1948 by Hughes *et al.* (*Memphis med. J.*, 1948, **23**, 116; *Abstracts of World Medicine*, 1949, **5**, 179)) is loaded with metal cartridges containing the desired sterile solution and, by means of a powerful spring plunger, forces the contents through a minute opening in a fine jet. This jet is apparently able to penetrate the skin, and thus no needles are employed and no sterilization is needed other than that of the skin and the nozzle of the injector.

In tests with this instrument the authors have recovered both trypan blue from the joints of cadavers and hydrocortisone acetate from the synovial fluid of living subjects. They also demonstrated radiographically the presence in the joint of diodone after jet injection of this substance, although a certain proportion of the medium usually remained in the periarticular or subcutaneous tissues.

They have injected all joints, except the shoulder and hip, of patients with rheumatoid arthritis, and have noted improvement in some 66% of cases. They state that the indications for hypospray injection are those for needle injection. One disadvantage of the method is that synovial fluid cannot be removed simultaneously. Cases of tenosynovitis and bursitis have also been treated. *J. Warwick Buckler*

1091. **The Value of Agglutination Reactions with Sheep's Erythrocytes Sensitized with an Immune Serum in the Classification of Chronic Inflammatory Rheumatism.** (Réactions d'agglutination des globules rouges de mouton sensibilisés par un immun sérum. Leur intérêt pour la classification des rhumatismes inflammatoires chroniques)

F. JACQUELINE, L. PODLIACHOUK, and A. EYQUEM. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **1**, 1092–1104, Dec., 1956. 44 refs.

This report details and analyses the authors' experiences with sheep-erythrocyte agglutination tests for rheumatoid arthritis carried out at the Rheumatism Research Centre, Aix-les-Bains, and the Institut Pasteur, Paris, in which they used a technique of sensitized sheep-cell agglutination after adsorption of heterophil agglutinins, similar to that of Svartz *et al.* and Heller *et al.*; a titre of 1 in 48 was taken as the dividing line between a negative and a positive result.

Out of a total of 707 tests on 642 patients or controls they found positive results as follows: rheumatoid arthritis (R.A.), including juvenile R.A., 265 out of 477; ankylosing spondylitis, 6 out of 124; gout, 1 out of 17; arthritis associated with psoriasis, 1 out of 13; rheumatic fever, *nil* out of 11; and in healthy control subjects, 2 out of 65. The test was more often positive in R.A. when nodules were present, but in 11 of the cases of R.A. with nodules the reaction was negative. There was a rough correlation between the agglutination titre in R.A. and the erythrocyte sedimentation rate, and also with the duration of disease, but none with loss of weight or with variations in the pattern of the serum proteins as revealed by paper electrophoresis. In 379 cases comparison of this technique with the Waaler–Rose technique, and in 351 sera with the "serum erythrocyte agglutination" technique of Heller *et al.*, showed it to be more reliable than either of these two methods. The test also helps to differentiate between the various symptoms of chronic polyarthritis. *A. St. J. Dixon*

1092. **Rheumatic Epicondylitis of the Humerus.** (Die rheumatische Epicondylitis humeri)
W. BELART. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **86**, 1279–1281, Nov. 10, 1956. 10 refs.

The author describes 100 cases (50 in males and 50 in females) of humeral epicondylitis seen in private practice in Zürich. Occupational strains accounted for only a few of them, but in 30 men and 35 women a history or physical signs of "rheumatic" pains elsewhere were obtained, mostly described as lumbago and fibrositis. Recurrences were common, in the opposite arm as well as in the same arm. Various clinical forms of the condition could be distinguished. Treatment consisted in the injection of tuberculin or injecting the lesion with hydrocortisone; the latter proved the more effective.
A. St. J. Dixon

1093. **A Study of the Evolution of Rheumatoid Arthritis.** (Eine Studie zur Entwicklung der primär chronischen Polyarthritis)
M. HUNZIKER and J. M. BIVETTI. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **86**, 1275–1279, Nov. 10, 1956. 11 figs., 11 refs.

The authors, basing their conclusions on the findings in 100 unselected cases of rheumatoid arthritis seen at the University Rheumatism Clinic, Zürich, including 31 in which the disease was of less than one year's duration, present a brief review of the onset and progress of this malady.

The proportion of patients showing the various classic signs of inflammation of their joints and the proportion with abnormal serum levels of iron, copper, streptococcal agglutinins, and antistreptolysin, are plotted against duration of the disease. This showed that the longer the duration, the greater the chance of the serum iron level being low [but otherwise no very impressive trends are shown].

The patients at this clinic are treated with amidopyrine or phenylbutazone, or alternatively with salicylates if the former drugs are not tolerated. Gold is given as a standard additional therapy and the schedule employed is described. Hormonal and physical methods of treatment are briefly set out.

The radiological findings in 532 instances, some of which are described and illustrated, included among others osteoporosis, erosions, and subperiosteal new bone formation. *A. St. J. Dixon*

1094. **A Comparative Therapeutic Trial in Rheumatoid Arthritis.** (Vergleichende Therapie der primär chronischen Polyarthritis)
B. SCHLEGEL, T. BEHREND, and M. EGGSTEIN. *Ärztliche Wochenschrift* [*Ärztl. Wschr.*] **11**, 1101–1107, Dec. 14, 1956. 3 figs., 37 refs.

At the University Clinic, Marburg–Lahn, 47 patients with rheumatoid arthritis in all different stages were first treated with salicylates (up to 10 g. daily for 3 weeks). Those who were unable to tolerate the treatment or did not respond favourably or eventually relapsed within one year were given phenylbutazone (400 mg. daily for 3 weeks). If this treatment failed an oral gold preparation, "aurubin", (2·7 mg. daily for 56 days) was then tried, and if this also failed the next treatment was ACTH (25 mg. daily for 10 days), or cortisone (50 mg. daily for 14 days), or prednisolone (10 mg. daily for 56 days). Finally, if all these treatments had failed, spa treatment with mud-baths was tried. The response to treatment was classified according to the criteria proposed by the American Rheumatology Association. As a result of these trials it was considered that spa treatment with mud-baths was the most successful. There were no controls.

[The value of this paper is greatly limited by the number of uncontrolled variables introduced and by the failure to allow for the time element; thus, although the last treatment was apparently the most successful, the benefit obtained could have been equally well attributed to spontaneous improvement during the period of the trial.] *G. W. Csonka*

1095. **Chloroquine and Rheumatoid Arthritis. A Short-term Controlled Trial**
A. FREEDMAN. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 251–257, Sept., 1956. 13 refs.

A controlled clinical trial of chloroquine in rheumatoid arthritis is reported from Hackney Hospital, London, 34 patients receiving tablets of chloroquine and 32 receiving tablets of similar appearance but containing inert material. The dosage of chloroquine varied from 200 to 300 mg. daily, and the trial lasted 16 weeks. The results of treatment were assessed from a number of factors, including joint tenderness, strength of grip, time taken to walk 40 yards (36·5 metres) or to insert a lace in and out of the holes on one side of a boot, the haemoglobin level, and the erythrocyte sedimentation rate (E.S.R.). Analysis of the figures for joint tenderness, grip, and lacing time showed significant improvement in the chloroquine-treated group, but only slight improvement, which was not significant, in the control group. No change was noted in either the haemoglobin level or the E.S.R. Euphoria and delusions developed in one elderly female patient receiving chloroquine, but it was not established that these were due to the drug; otherwise no serious toxic effects were observed.

The author concludes that the results, although not providing conclusive evidence of the long-term value of chloroquine in rheumatoid arthritis, indicate that further investigation is warranted. *C. E. Quin*

1096. **Rheumatoid Arthritis and the Positive L.E.-cell Phenomenon**
J. H. KIEVITS, J. GOSLINGS, H. R. E. SCHUIT, and W. HIJMANS. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 211–216, Sept., 1956. 16 refs.

If the blood in a case of rheumatoid arthritis exhibits a positive L.E.-cell phenomenon, should the disease in this case invariably be regarded as an oligosymptomatic form of systemic lupus erythematosus? This problem, has been investigated at the University Hospital, Leiden, Netherlands, where a positive L.E.-cell phenomenon was obtained in 17% of 488 cases of rheumatoid arthritis,

whereas in control series totalling 644 patients L.E. cells were found only in association with clinical findings compatible with a diagnosis of systemic lupus erythematosus, rheumatoid arthritis, or (in one case) scleroderma. Among those giving a positive reaction in the former group there was a significantly higher incidence of splenomegaly, abnormal urinary sediment, false positive serological reactions for syphilis, and a high erythrocyte sedimentation rate which failed to fall under gold therapy than in those cases in which the L.E.-cell test gave a negative result. On the other hand in a number of individual cases of rheumatoid arthritis the positive L.E.-cell phenomenon was not related to a typical clinical picture of lupus erythematosus, and the authors do not consider that these cases can be labelled as systemic lupus erythematosus. They suggest that the results of the test be treated as purely descriptive, and that while patients with rheumatoid arthritis with a positive L.E.-cell phenomenon tend to differ, as a group, in certain respects from those without, the present state of knowledge does not permit any dogmatic conclusion concerning the diagnostic significance of this finding in rheumatoid arthritis. *E. G. Rees*

1097. **Nature of Anaemia in Rheumatoid Arthritis. III. Changes in the Bone Marrow and Their Relation to Other Features of the Disease**
J. Richmond, D. L. Gardner, L. M. H. Roy, and J. J. R. Duthie. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 217–226, Sept., 1956. 2 figs., 41 refs.

The authors have studied the iron content and cytology of the bone marrow and the peripheral blood picture in 64 cases of rheumatoid arthritis seen at the Northern General Hospital, Edinburgh. A firm diagnosis of rheumatoid arthritis had been made in each case, and all cases of anaemia due to blood loss were excluded. The ages of the patients ranged from 20 to 79 (mean 53) years, the average duration of the disease was 8 years, and in all but 3 of the patients its degree of activity was graded as " very active " or " moderately active ". All patients were receiving the same basic treatment of bed rest, physiotherapy, and salicylates in hospital.

The iron content of the bone marrow was estimated by the Prussian-blue reaction in 61 cases, in 19 (31%) of which no stainable iron was found. A chemical method which measured all the non-haem iron in the sample (as opposed only to the iron in haemosiderin) showed iron in measurable amounts in all of 32 specimens of marrow examined. There was no correlation between the amount of iron in the marrow, measured by either method, and the haemoglobin level, the erythrocyte count, the mean corpuscular haemoglobin concentration, the erythrocyte sedimentation rate (Westergren), or the plasma iron level. However, the erythrocyte sedimentation rate and the haemoglobin level were correlated significantly.

The cytology of the bone marrow in 60 cases was studied independently by two observers. Only normal architecture was found, there being no evidence of reticulo-endothelial hyperplasia. A slight increase in the proportion of plasma cells above their normal of 2·1%, observed in one-third of the cases, was significantly related to the serum globulin level. The normoblast count was directly related to the haemoglobin level, this relationship being particularly marked when cases of disease of short duration were excluded. Thus it is suggested that the marrow fails to respond adequately to prevent anaemia in the later stages of the disease.

The authors conclude that while the severity of the anaemia in rheumatoid arthritis closely parallels the degree and duration of activity of the disease, the anaemia is not due solely to a deficiency of iron in the marrow. *J. Warwick Buckler*

1098. **Growth in Still's Disease**
B. M. Ansell and E. G. L. Bywaters. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 295–319, Dec., 1956. 29 figs., bibliography.

At the Canadian Red Cross Memorial Hospital, Taplow, Buckinghamshire, a survey was undertaken of the height, weight, and bone growth in 119 patients suffering from Still's disease. It was found that in this disease, as in other chronic diseases of childhood, growth in height and weight was retarded. Over a period of 5 years height in approximately half the patients was more than 10% below the normal. When the disease was quiescent, however, growth in many of the younger children was rapidly resumed and returned to standard values. Weight was lost at the onset of the illness, but returned to normal with quiescence of the disease. There were pronounced residual defects in height and weight among children with fever and prolonged disease activity. Height was much less frequently affected than weight.

In the neighbourhood of affected joints there were abnormalities of bone development, including premature epiphysial fusion, increase in epiphysial size and in longitudinal growth of the metaphysis, and minor changes such as periostitis. Abnormal subperiosteal bone accretions occurred in the early stages of the disease and tended to become reabsorbed later on. Radiographs in 3 cases revealed dense white bands beneath the epiphysial line resembling lead or bismuth lines. Unilateral arthritis of the wrist was found in 5 patients and maldevelopment of the lower jaw in 22. Retarded development of the secondary sex characteristics was observed in cases of moderately severe disease. Administration of male sex hormones in some cases resulted in a rapid gain in weight, while cortisone therapy caused temporary obesity and slowing of growth. There was little apparent effect on skeletal maturation. *A. Garland*

1099. **A Report of Experience in 1,080 Cases of Ankylosing Spondylitis.** (Erfahrungsbericht über 1080 Fälle von chronisch-versteifendem Wirbelsäulenrheumatismus (Spondylarthritis ankylopoetica, Morbus Bechterew))
W. Treiber. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **86**, 1283–1287, Nov. 10, 1956. 3 figs., 23 refs.

The author describes the findings in 1,080 cases of ankylosing spondylitis treated at the Sanatorium for Rheumatism, Bad Bramstedt, Holstein. Predisposing factors included head lesions (38·1% of cases), trauma to

the spine (8·8%), gonorrhoea and other venereal conditions (4·5%), and intestinal diseases such as dysentery or typhoid (4·5%). In 67% the disease started between the ages of 21 and 40, but the lowest age of onset was 9 years and the latest 64. Only 6·7% of the patients were women. In 0·7% of cases other members of the patient's family were affected. It was found that determination of the serum protein pattern was helpful in the diagnosis of the disease. The results of treatment were assessed by noting any increase in body height, chest expansion, and minimum finger-to-floor distance. The results of hydrotherapy combined with injections of a proprietary muscle relaxant (" iralgin ") into the sacrospinalis muscle are compared with those obtained from hydrotherapy combined with other forms of treatment, including radiotherapy [but these methods show no significant improvement in the objective tests].

The author concludes from this study that permanent improvement can be achieved only through planned long-term collaboration between the family doctor and the specialist. *A. St. J. Dixon*

COLLAGEN DISEASES

1100. Collagen Disease of the Small Bowel

I. MARSHALL. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 978–983, Nov. 22, 1956. 9 figs., 15 refs.

The author of this paper from Jersey City Medical Center, New Jersey, states it as his purpose " to report this condition [collagen disease of the small bowel] in its early and late stages so that it can be readily recognized clinically in the operating room and possibly treated earlier ". Full details of 3 cases are presented; Case 1 was in a man of 47 years, Case 2 in a negress aged 35, and Case 3 in a man aged 23. All 3 patients presented with upper abdominal pain of a duration of 6 months to one year. This was related to food in Cases 1 and 3, and was accompanied by abdominal distension in Cases 2 and 3, by vomiting in Cases 1 and 2, and by nausea only in Case 3. Bowel action was normal in Cases 1 and 3, while diarrhoea and melena occurred in Case 2. Loss of weight was complained of in all cases, the loss varying from 10 lb. to 23 lb. (4·5 to 10·4 kg.). Physical examination revealed little except evidence of weight loss in Cases 1 and 2, while there was diffuse epigastric tenderness with slight guarding in Case 3. All 3 patients underwent exploratory laparotomy. Surgical treatment in Case 1 consisted in intestinal resection and anastomosis; the patient survived, but the long-term benefit is considered to require time and also many more recorded cases to elucidate. In Case 2 the patient's condition deteriorated, and she died 2½ years later following resection of a small piece of bowel for biopsy. In Case 3 the disease was found to be so widespread as to render definitive intervention impossible, and a biopsy only was taken.

The diagnosis of collagen disease of the small bowel is discussed on the basis of the above cases. The condition may be accompanied by scleroderma or Raynaud's phenomenon. Diagnosis is suggested by the characteristic *x*-ray findings of dilated bowel, with barium retention and diminished peristalsis, but these signs are not always present. The gross appearances of the early stages include oedema, diminished tone and peristalsis, increased calibre of the bowel, dilated radial lymphatics filled with a white substance, and enlarged soft lymph nodes. Later the small bowel shows a white, sclerosed serosal surface, diminished tone and peristalsis, and hard lymph nodes. Free peritoneal fluid was not seen in any of the cases.

Confirmation of the diagnosis rests on the microscopical demonstration of replacement of the muscularis and subserosal and submucosal infiltration by collagen. Post-mortem examination may reveal sclerosis of the heart, kidneys, spleen, or bone. *L. G. Fallows*

1101. Corticotrophin and Cortisone Therapy in Dermatomyositis

M. MCELLIGOTT. *British Medical Journal* [*Brit. med. J.*] **2**, 1509–1511, Dec. 29, 1956. 23 refs.

The author of this communication reports the results of treatment with corticotrophin or cortisone of 3 cases (all in females) of dermatomyositis at Newcastle General Hospital. The first patient, aged 30, presented with a widespread myositis and facial erythema. The disease progressed rapidly despite administration of antibiotics and salicylates. Response to corticotrophin treatment was prompt and dramatic, the patient surviving an abortion accompanied by considerable uterine haemorrhage during its course. Treatment was discontinued after a total of 5 g. of corticotrophin had been given, at which time recovery was complete. The second patient, aged 49, was admitted with extensive myositis, and later developed lower motor neurone lesions of both hands. The disease was further complicated by a severe purulent bronchitis. Urinary creatine excretion was within normal limits. Again antibiotics proved unsuccessful, but there was a rapid and apparently complete recovery following treatment with corticotrophin to a total dosage of 2·2 g. The third patient, aged 47, was admitted in a critical state and was immobilized by extensive muscle involvement. Urinary creatine excretion was raised, and muscle biopsy showed oedema and round-celled infiltrates. A good response to corticotrophin was obtained in the initial stages of the disease, but later both soft-palate palsy and inhalation pneumonia developed and the patient died.

After a comprehensive review of the literature the author concludes that corticotrophin may be life-saving in acute fulminating dermatomyositis; it is, however, less useful in the more chronic form of the disease, though in view of the occasional success claimed in this category it should never be withheld.

J. N. Harris-Jones

1102. Present Status of Allergy in the Connective Tissue Diseases

F. B. MURPHEY. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **50**, 57–62, Jan., 1957. 12 refs.

Neurology and Neurosurgery

1103. **A Neuropathic Syndrome of Uncertain Origin. Review of 100 Cases**
E. K. CRUICKSHANK. *West Indian Medical Journal* [*W. Indian med. J.*] **5**, 147–158, Sept., 1956. 2 figs., 30 refs.

The author reports on 100 cases of the neurological syndrome described by Scott in 1918 as "central neuritis" which occurred in 55 male and 45 female patients studied at the University College Hospital of the West Indies since 1953. This disease, which is of unknown aetiology, was first described in 1888 in Jamaica. Since then a similar syndrome has been described in various countries, notably among European prisoners-of-war held by the Japanese in the Far East during the second world war. The syndrome is characterized by symptoms attributable to (1) upper motor neurone lesions; (2) damage to the first sensory neurone in the peripheral nerves or posterior columns or both; (3) retrobulbar neuritis; and (4) eighth nerve deafness, the symptoms occurring in this order of frequency.

The onset was gradual in all except 11 of the author's cases, the commonest presenting symptom being weakness of the lower limbs. Sensory changes could be demonstrated in 54 cases, although subjective symptoms occurred in only 22 cases. Ten patients complained of a burning sensation in the feet and 19 of lumbar pain. Disturbances of micturition were noted in 61 cases. Some degree of optic atrophy with scotomata was noted in 26 cases and temporal pallor of the optic disk in 29 cases. Histamine-fast achlorhydria was found in 25 of 90 cases examined and 3 of these showed a megaloblastic bone-marrow reaction. No histological studies were performed in any of these cases.

The author compares these findings with those reported in prisoners-of-war, where dietary deficiency was undoubtedly the chief aetiological agent. Reviewing his own cases he finds that the diet was poor in less than half. He considers that the symptoms point to demyelinating lesions in the long axons of the pyramidal cells and first sensory neurones; these are phylogenetically the most recently evolved tracts in the cord. Discussing the aetiology, he notes that while a dietary deficiency is a likely cause, a toxic factor, as in lathyrism, cannot be excluded. *William Hughes*

1104. **Great Auricular Neurotomy for Tic Douloureux. A Controlled Clinical Trial**
J. PENMAN and L. S. WALSH. *British Medical Journal* [*Brit. med. J.*] **1**, 22–25, Jan. 5, 1957. 3 refs.

A carefully conducted controlled clinical trial embracing 60 cases has led the authors to conclude that there is no foundation for the claim that section of the great auricular nerve has any effect on tic douloureux.
L. Crome

DIAGNOSTIC METHODS

1105. **Electrical Signs in the Diagnosis of Carpal Tunnel and Related Syndromes**
J. A. SIMPSON. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 275–280, Nov., 1956. 5 figs., 10 refs.

The author describes a method of electrodiagnosis applicable to the carpal-tunnel and allied syndromes which he has investigated at the National Hospital, Queen Square, London. He points out that hitherto electromyographic diagnosis has depended upon the demonstration of partial denervation confined to the muscles supplied by a particular motor nerve or one of its branches. As the pathological basis of the carpal-tunnel syndrome is assumed to be a localized ischaemic lesion of peripheral nerve the author set out to determine whether phenomena known to be present in experimental ischaemia of short lengths of nerves could be demonstrated in patients with the syndrome. The two phenomena investigated were (1) diminished velocity of nerve impulse conduction in the ischaemic segment and (2) repetitive firing of motor nerve fibres after a single shock stimulus; 17 patients were examined, 15 with the carpal-tunnel syndrome and 2 with lesions of the ulnar nerve, and as controls 10 healthy subjects, 5 patients with motor neurone disease, and 10 with various muscular disease were selected.

The technique employed was as follows. Cathodal stimulation was applied along the course of a nerve with a brief condenser discharge (time constant 20 microseconds) which was triggered by the time-scale of a recording oscillograph at a point indicated on it. Threshold or supramaximal stimuli were applied once per second. Electromyographic recordings were made through coaxial needle electrodes inserted into the abductor pollicis brevis or opponens pollicis muscles for median-nerve, and the abductor digiti minimi or first dorsal interosseous muscles for ulnar-nerve conduction studies. The action potentials after suitable amplification were displayed on one beam of a double-beam cathode-ray oscillograph, with the second beam recording a time-scale. Ten sweeps were recorded on the photographic record. The time interval between the recorded stimulus artefact and the initial deflection of the summated action potential was measured at each site of stimulation. The length of nerve from stimulating to recording electrode was estimated by surface measurement.

Slowing of the conduction time was demonstrated in the presumed ischaemic segment of the median nerve in 11 out of the 15 cases of carpal-tunnel syndrome, with return to normal after operative decompression in 3 cases. Repetitive firing of motor units after single shock stimula-

tion was present in 7 out of the 15 cases. Increased temporal dispersion of the summated action potential of the muscle supplied by the affected nerve returned to normal after decompression. In a patient with chronic traumatic neuritis of the ulnar nerve at the elbow slowed conduction was shown to be confined to the damaged segment. In a patient with neuritis of the deep branch of the ulnar nerve it was demonstrated that the conduction block was confined to the fibres supplying the first dorsal interosseous muscle, the branch to the abductor digiti minimi muscle escaping.

The author suggests that the incidence of positive findings in this small series of cases indicates that demonstration of the changes described will be of value as a confirmatory test for ischaemic nerve block.

Kenneth Tyler

BRAIN AND MENINGES

1106. **Brain Swelling of Unknown Cause**
A. L. SAHS and R. J. JOYNT. *Neurology* [*Neurology*] **6**, 791–803, Nov., 1956. 10 figs., 26 refs.

Having previously reported, in 1939, 5 cases of swelling of the brain of unknown aetiology, the authors now describe 17 further cases which they have studied at the State University of Iowa College of Medicine, Iowa City, during the past 16 years. The condition has been variously termed pseudotumor cerebri, serous meningitis, otitic hydrocephalus, toxic hydrocephalus, and other names; since it is rarely fatal there have been no previous histological studies. A review of the literature shows that ventriculography usually reveals no distension of the ventricles, and although intracranial pressure is high, the actual amount of subarachnoid fluid is decreased. The essential clinical features are headache and visual disturbances, amounting in some cases to visual failure or diplopia.

In the present series of 12 women and 5 men headache was present in every case, diplopia in 7, and vomiting in 8 cases. The blood pressure was not raised. Papilloedema was observed in every case and was observed to subside or disappear during recovery. Retinal haemorrhages were seen in 8 cases. An interesting observation was that 10 of the 11 cases occurring after puberty were in obese women, and the increased incidence of obesity in such cases has been noted by other observers. Histological examination of biopsy specimens of the brain, obtained in 10 cases, revealed both intra- and extracellular oedema. In one case in which the superior sagittal sinus was thrombosed there was scirrhous carcinoma of the breast, with metastasis in the skull. In another case, however, the superior sagittal and lateral sinuses were both patent. The cellular and protein content of the cerebrospinal fluid was usually normal, but the pressure was raised. In 8 of the authors' cases there had been an infectious disease within 2 months of the onset of the condition, and in 3 of these there had been in addition infection of the ear. The authors note that the aetiology of the condition is still unknown. The important thing in diagnosis is to exclude the more serious conditions which can be confused with pseudotumor cerebri. There is no specific treatment and all genuine cases recover spontaneously, but it is wise to keep them under clinical observation as long as necessary.

William Hughes

1107. **Cerebral Manifestations of Vitamin-B_{12} Deficiency**
J. MACD. HOLMES. *British Medical Journal* [*Brit. med. J.*] **2**, 1394–1398, Dec. 15, 1956. 19 refs.

Changes in the nervous system due to deficiency of vitamin B_{12} (cyanocobalamin) may affect the spinal cord, peripheral nerves, or the brain. In a series of 25 such cases seen at the Midland Centre for Neurosurgery, Birmingham, in the past few years, pronounced cerebral symptoms were present in 14. A histamine-fast achlorhydria and signs of spinal-cord or peripheral-nerve involvement were found in all 14 cases, and in 13 there was a megaloblastic reaction in the bone marrow. Slowing of mental processes, confusion, and memory defect were constant features, and other cerebral manifestations included delusions or visual or auditory hallucinations in 8 cases, depression in 7, dimness of vision due to optic atrophy in 3, and epilepsy, dysphasia, and extreme agitation or maniacal behaviour in 2 each. In 4 of the patients the psychological symptoms preceded the onset of anaemia or of the other neurological signs by periods ranging from 2 to 8 years.

Intensive treatment with cyanocobalamin (1,000 μg. initially, followed by 500 μg. twice weekly) resulted in a marked improvement in the mental symptoms in 11 of the 14 cases. At necropsy on 2 of the patients who died the histological changes observed in the cerebral white matter were similar to the diffuse and focal areas of degeneration noted in the spinal cord in subacute combined degeneration. The author emphasizes the need for early diagnosis in such cases if treatment is to be effective. It is suggested that determination of the serum cyanocobalamin concentration and the performance of gastric biopsy may prove of value in doubtful cases in which the peripheral blood and bone marrow present an apparently normal picture.

A. G. Freeman

1108. **Sensory Deficits in Visual Agnosis**
G. ETTLINGER. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 297–307, Nov., 1956. 2 figs., 14 refs.

In the studies here reported from the Institute of Neurology, Queen Square, London, the author set out to test the view of the German worker Bay (*Brain*, 1953, **76**, 515) that visual agnosia is not a specific entity, but is dependent on visual defects which may not be detectable on routine perimetry. For this purpose apparatus was devised [for a description of which the original paper must be consulted] to test brightness discrimination, flicker fusion, acuity for small objects, local adaptation, tachistoscopic acuity, and perception of apparent movement, a total of 30 patients with "brain lesions" being investigated; of these, 12 had neither visual nor perceptual difficulties, 10 had field defects but showed no evidence of visual agnosia, while the remaining 8 showed both field defects and various types of higher perceptual disorder.

In the first 12 cases the tests showed some degree of sensory deficit in the absence of visual field defects, and in 10 of the cases with field defects more obvious sensory deficits were found. On the other hand in the 8 cases with higher perceptual defects there was no significant increase in the sensory deficit and no example of a true visual agnosia, although one patient showed " prosopagnosia ". In this last case the sensory efficiency was low, as would be expected from Bay's theory, but in 3 other cases with even lower indices of sensory efficiency there was no prosopagnosia. It was noted that when sensory defects were combined with intellectual loss, agnosia was not present, again contradicting Bay's theory.

The author concludes that although impaired visual discrimination is often associated with disturbances of visual perception, it is not in itself sufficient to give rise to agnosia. Bay's reliance on the method of adaptation is criticized; nevertheless confirmation was obtained for his finding that bilateral defects of visual discrimination can result from a unilateral lesion. *L. G. Kiloh*

1109. **Studies on Headache. Central versus Peripheral Action of Ergotamine Tartrate and Its Relevance to the Therapy of Migraine Headache**

E. PICHLER, A. M. OSTFELD, H. GOODELL, and H. G. WOLFF. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **76**, 571–577, Dec., 1956. 2 figs., 20 refs.

In an investigation carried out at the New York Hospital (Cornell Medical College), young healthy male subjects were given 0·5 mg. of ergotamine tartrate intravenously. This produced marked peripheral vasoconstriction followed 15 minutes later by nausea. The response to the cold pressor test in 6 experiments on 5 subjects was unaltered, and the carotid sinus reflex was uninfluenced in 8 experiments on 5 subjects. There was no alteration in the bradycardia produced by the infusion of L-noradrenaline in 6 experiments on 6 subjects. " Hydergine " given before or after ergotamine tartrate in 3 experiments did not alter the vasoconstrictor effect of the latter drug. In 2 patients whose temporal arteries had been denervated by cervical sympathectomy ergotamine tartrate still produced peripheral vasoconstriction.

From these results the authors conclude that in the usual therapeutic dosage ergotamine tartrate terminates an attack of migraine by means of its peripheral effect, and that the central effects are not significant.

I. Ansell

1110. **Communicating Hydrocephalus from Subarachnoid Bleeding**

E. L. FOLTZ and A. A. WARD. *Journal of Neurosurgery* [*J. Neurosurg.*] **13**, 546–566, Nov., 1956. 7 figs., 15 refs.

The authors report from the University of Washington, Seattle, that in the last 3 years communicating hydrocephalus has developed in 10 cases after bleeding into the basal cisterns following trauma, operative haemorrhage, or rupture of an intracranial aneurysm. The clinical features are described and the wide variability of symptoms, the most common of which was headache, is noted. Diagnosis in such cases is established by encephalography. It was noteworthy that papilloedema was present in one case only, and its rarity may possibly be accounted for by fibrosis of the perineural spaces around the optic nerve. *L. Crome*

1111. **The Treatment of Narcolepsy with Methyl Phenylpiperidylacetate: a Preliminary Report**

D. D. DALY and R. E. YOSS. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **31**, 620–626, Nov. 14, 1956. 3 refs.

Methyl phenidate (" ritalin ") was tried at the Mayo Clinic in the treatment of 36 patients suffering from narcolepsy, cataplexy, sleep paralysis, or hypnagogic hallucinations, 25 being followed up for periods varying from 5 weeks to 6 months. All other medication was stopped during administration of the drug, which was given in daily doses of 20 to 240 mg., in most cases from 60 to 80 mg.

Of the 25 patients followed up 21 reported " good " to " excellent " results, 2 showed minimal improvement only, and 2 were not benefited. All the 21 patients who responded well considered that the drug was superior to any other analeptic tried. Undesirable side-effects, including insomnia, nervousness, slight anorexia, anxiety, dryness of the mouth, rashes, and excessive perspiration, were noted by 13 patients; they occurred mostly in the early stages of treatment and did not call for cessation of the drug.

The authors consider that methyl phenidate is at present the drug of choice in the treatment of narcolepsy, and merits further investigation. *Marcel Malden*

1112. **Shift to Older Age Distribution in Parkinsonism. A Report on 1,000 Patients Covering the Past Decade from Three Centers**

R. S. SCHWAB, L. J. DOSHAY, H. GARLAND, P. BRADSHAW, E. GARVEY, and B. CRAWFORD. *Neurology* [*Neurology*] **6**, 783–790, Nov., 1956. 5 figs., 4 refs.

The authors present a report on an apparent change in the age distribution of Parkinson's disease, as observed in patients attending neurological clinics in the U.S.A. (Boston and New York) and Great Britain (Leeds) during the years 1948 and 1955. The investigation had its origin in the authors' observation that when 252 Parkinsonian patients attending Massachusetts General Hospital, Boston, in 1948 were grouped by age the distribution showed a clear peak of 77 patients between the ages of 50 and 59 years, whereas the age distribution of 331 such patients seen in 1955, 7 years later, showed the peak (114 cases) to occur between the ages of 60 and 69.

The investigation was therefore extended transatlantically and with the help of neurological colleagues in New York and Leeds the authors were able to extend their observations to cover a total of 466 patients seen in 1948 and 1,147 seen in 1955, for 818 of whom the date of onset of Parkinsonian symptoms could definitely be established. A graph relating incidence of cases to the lapse of years after an attack of, or exposure to, influenza

or encephalitis during the epidemic years 1917–26 (or where no exact history could be obtained, the arbitrary date 1920) resulted in a curve which showed a peak at 30 to 35 years after the time of exposure and then fell abruptly. This fall correlated with the finding at all three centres, at which also it was observed that fewer new cases of Parkinsonism are being seen and the peak in age distribution has shifted to the right, the age distribution curves for the three centres being essentially the same in 1948 and again in 1955. The figures show that the maximum incidence of Parkinsonism was in those born between the years 1885 and 1895, and it is notable that none of the 1,147 patients in the total series was born after 1926. Control studies of age distribution curves for non-Parkinsonian cases at the neurological clinics showed no such shift to the right. The indications are that two-thirds of this series of cases of Parkinsonism bore some relationship to the 1917–26 epidemic of influenza and encephalitis; if this is confirmed there should be a considerable fall in the number of cases of this disease in the next 10 years.

William Hughes

SPINAL CORD

1113. **Recovery of Function and Regeneration of Conduction Fibres in Traumatic Injuries of the Spinal Cord.** (Восстановление нарушенных функций и регенерация проводников при травматических повреждениях спинного мозга)
L. M. Dukhovnikova. *Советская Медицина* [*Sovetsk. Med.*] 65–68, No. 11, Nov., 1956.

Total transverse division of the spinal cord is always a serious condition and leads to lifelong invalidism. Although contemporary neuropathologists hold that recovery of motor, sensory, and trophic functions is impossible because the fibres of the central nervous system do not regenerate, the author denies that this is always the case, basing her assertion on the observation of 100 cases among which recovery of function occurred in 2—although one of the patients later died of urinary sepsis. In 10 cases histological examination carried out after death at various periods after the initial injury showed that on a background of degenerative change a new formation of nerve fibres was proceeding. Thus in cases examined 2 or 3 days after injury only degenerative changes were found, but in those examined after a period of about 3 weeks organization of the injured tissue was taking place. On the outer edges of the focus there was observed on the thickened and swollen axons the formation of collaterals, retraction spheres, and bulbs of the type described by Cajal. Over the next 3 months or more (the so-called intermediate period) scar tissue formed in the site of the necrotic focus, while outside this could be observed a disordered, fan-like distribution of nerve fibrils. Some axons, weaving, twisting, and retracing their direction, formed spirals suggestive of those of Peroncitto; in others sprouts or spiral swellings formed at the ends of the bulbs, thence passing through the scar tissue in various directions and often following the course of blood vessels. In the conducting tracts of the spinal cord regeneration of nerve fibres takes place above the lesion in the ascending tracts, and below it in the descending tracts. In the later stages the axon fibres become covered with a myelin sheath.

The author insists that the prognosis in these cases is not hopeless, but agrees that prolonged, persistent, and individualized treatment is necessary. The one patient who made a good recovery had sustained his injury 7 years before coming under observation and the intensive treatment lasted a further 2 years. At the end of this period he had recovered voluntary control of the flexor, adductor, and abductor muscles moving the hip-joints and of the flexor and extensor muscles of the knees; he could walk with crutches, and was conscious of the desire to micturate, although apparently control of micturition and defaecation were imperfect. In these cases urinary sepsis and bedsores are the greatest dangers after the early critical days. Physiotherapy and electrotherapy can play an important role in maintaining the functions of the limbs during the regenerative period.

L. Firman-Edwards

1114. **Arterial Pressure in Syringomyelia.** (Состояние артериального давления при сирингомиэлии)
G. G. Sokolyanskiĭ and A. E. Melerovich. *Советская Медицина* [*Sovetsk. Med.*] 18–23, No. 11, Nov., 1956.

The examination of 219 cases of syringomyelia showed that arterial hypotension was present in 40% and some degree of lowered blood pressure in 52·5% of the cases. The authors define hypotension as a systolic pressure below 100 mm. Hg and a diastolic pressure below 60 mm. Hg. A raised arterial pressure (that is, above the normal systolic maximum of 140 mm. Hg) was found in 4·1% of the cases. Asymmetry of the blood-pressure levels on the two sides of the body was often observed. Normally the difference in pressure between the right and left arm does not exceed 5 mm. Hg, but in only 88 out of these 219 patients was the difference less than 10 mm. The asymmetry was more often observed in cases in which the neurological signs pointed to a predominantly unilateral lesion, hypotonia being more marked on the side of the lesion. There was no parallelism between the systolic and diastolic changes in pressure; thus in one case of involvement of the spinal cord from the 1st cervical to the 10th dorsal roots and with symptoms of syringobulbia involving the facial nerve the blood pressures were 95/85 and 105/65 mm. Hg on the right and left sides respectively, the systolic pressure being 10 mm. higher and the diastolic pressure 20 mm. lower on the left side. In 16 cases the greater reduction in the systolic pressure was on the side opposite to the lesion.

It is suggested that these phenomena are probably due either to pressure on the lateral horns of the spinal cord, where the vasoconstrictor impulses arise, or to pressure on the vasodilator fibres arising from the base of the posterior horn. In bulbar cases the vasomotor centre in the medulla is probably involved. Successful treatment of the disease may, and in some of the present cases did, lead to a return of these pressure changes to normal.

L. Firman-Edwards

Psychiatry

1115. **Chromosomal Sex and Psychosexuality.** (Chromosomengeschlecht und Psychosexualität)
M. BLEULER and H. R. WIEDEMANN. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **195**, 14–19, 1956. 38 refs.

The purpose of the investigation here reported from the University Psychiatric Clinic, Zürich, was to determine whether the chromosomal sex of homosexuals and transvestites concords with their somatic or with their psychic sexuality. The authors carried out the two parts of the investigation separately, one of them obtaining blood smears from normal subjects and homosexuals, the other, ignorant of the origin of these smears, determining their chromosomal sex by examination of the nucleus of polymorphonuclear leucocytes in the blood films. It was found that in all cases the somatic sex followed the chromosomal sex.

In the same way an investigation of 20 male and 2 female homosexuals of long standing showed that the chromosomal sex of all these subjects corresponded to their somatic sexuality, as was the case also in 9 severe cases of transvestism, 5 in males and 4 in females. The authors conclude that psychosexual development is independent of chromosomal sex. However they stress that the negative findings in this investigation leave the question of the explanation of homosexuality wide open and that they should not be interpreted as proof of its exclusive psychogenesis. *F. Letemendia*

1116. **Benactyzine as an Aid in Treatment of Anxiety States. Preliminary Report**
G. R. HARGREAVES, M. HAMILTON, and J. M. ROBERTS. *British Medical Journal* [*Brit. med. J.*] **1**, 306–310, Feb. 9, 1957. 10 refs.

In order to test the therapeutic efficacy of benactyzine hydrochloride (" suavitil ") the authors carried out, at the General Infirmary at Leeds, a "double blind" controlled investigation on 31 psychoneurotic out-patients aged between 20 and 65 suffering from anxiety states of less than 4 years' duration; patients with severe anxiety and marked depressive symptoms were excluded.

Each patient received inert tablets for 2 weeks. His symptoms were then assessed independently by two psychiatrists using a 13-item list of anxiety manifestations, each item being rated on a 5-point scale. The correlation between the two assessments was very high ($r=0{\cdot}89$). During the next 3 weeks the patients received either active or inert tablets according to a random code known only to the hospital pharmacist. The dosage was increased by one tablet a day to a maximum of 2 tablets four times a day. At the end of this period the same psychiatrists again assessed the patients' clinical state independently.

During the blind-trial period 6 patients were eliminated because their life situation had changed in such a way as to account for an observed improvement in 5 of them and a slight deterioration in one. This left 12 control and 14 experimental subjects. An assessment of " global " improvement showed no difference between the two groups of patients. The 13-item list of manifestations of anxiety, however, which allowed a more refined assessment, indicated that the average degree of improvement was greater among the patients who received benactyzine tablets than among those receiving inert tablets, the difference being statistically significant if the improvement was measured as the percentage reduction of the initial anxiety score ($P=0{\cdot}06$). In more than half the patients benactyzine produced side-effects, mainly in the form of dizziness and " muddled thinking ". Depressive symptoms, however, were not increased by the drug.

[The authors emphasize that double-blind controlled investigations and improved methods of assessment of the patients' clinical condition are essential in studying the effects of drugs " in order to circumvent the capacity for unwitting self-deception " on the part of the investigators. It is doubtful, however, whether the authors have succeeded in escaping self-deception. They state that " even after the rejection from our series of patients in whom improvement appeared to result from a favourable change in their life situation ", they still found improvement in three-quarters of their control patients. Nevertheless, after the trial was over it was found that the 5 patients with a favourable change in their life situation had been receiving inert tablets and the patient who had deteriorated had received benactyzine. That every elimination of a patient because of a changed life situation should have favoured the evidence that benactyzine is therapeutically effective could have happened by chance only about 16 times in 1,000 investigations; it is therefore not likely to have happened by chance. It is more probable that therapeutic trials of this kind cannot be entirely " blind " as the clinical effects of the drug are typical and can be differentiated from neurotic phenomena.] *F. K. Taylor*

1117. **Benactyzine in Psychoneurosis: a Controlled Clinical Trial in Hospital Patients**
C. P. SEAGER and A. LEITCH. *British Medical Journal* [*Brit. med. J.*] **2**, 1407–1409, Dec. 15, 1956. 11 refs.

The authors report from Barrow Hospital, near Bristol, the results of a controlled trial of benactyzine hydrochloride in the treatment of psychoneurosis. Initially 16 in-patients in whom anxiety and tension were prominent symptoms were selected for the trial, but only 13 completed it, further administration of the drug in 2 cases being considered inadvisable because of its depressive effect. Benactyzine was given in a dosage of 2 mg. 3 times a day for a period not exceeding 2 weeks, and an inert placebo for another 2 weeks, a double-blind

method of control being employed. The five-point rating scales used in assessing the efficacy of the drug covered various symptoms, ranging from anxiety and tension to general condition and depression. Daily recordings were made by the patients themselves, the nursing staff noted degrees of restlessness and hours of sleep, and clinical signs and symptoms were assessed bi-weekly by the medical staff. The electroencephalogram was recorded before and twice during the course of the trial.

The results indicated that benactyzine gave no better results than the placebo. The authors conclude that benactyzine was not effective for the relief of tension in the 13 patients studied. *John A. Clark*

1118. **The Mild Endogenous Depression**
C. A. H. WATTS. *British Medical Journal* [*Brit. med. J.*] **1**, 4–8, Jan. 5, 1957. 4 refs.

The author, a general practitioner with psychiatric experience, has already shown that mild endogenous depression is essentially a disease of general practice (*Brit. med. J.*, 1956, **1**, 1392; *Abstracts of World Medicine*, 1956, **20**, 478). Only about one-sixth of the cases are symptomatically of the severe " mental-hospital " type. An analysis of the presenting symptoms in 100 cases showed that in at least 40% the picture was one of possible organic disease, and even in some of the cases with predominantly psychiatric symptoms the picture was not classic.

The author divides cases into 4 groups: Group 1, overt depression; Group 2, depression disguised as an anxiety state; Group 3, " depressive equivalent "—that is, the depression simulates organic illness; and Group 4, depressive grafts, where symptoms of endogenous depression are superimposed on organic illness. Cases illustrative of each group are described. Modifications of traditional symptomatology are discussed in terms of difficulty in thinking, the depression itself (including suicidal ideas, phobias and obsessions, and insomnia), and psychomotor retardation. The " injured bewilderment " of the patient and the transference relationship are also discussed. In the author's view the doctor should be able to treat many of these cases—by sedation where needed, by euphoriants or hormones, and, above all, by sympathetic reassurance and understanding until spontaneous remission takes place. Increasing depth of depression, suicidal ideas, secondary psychotic symptoms, or prolonged duration of a mild illness (beyond 3 months) are indications for psychiatric advice and, possibly, electric convulsion therapy. [This is excellent clinical material of a type rarely published on an important diagnostic problem.] *A. C. Tait*

1119. **Inappropriate Affect**
A. HARRIS and M. METCALFE. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 308–313, Nov., 1956. 38 refs.

Having satisfied themselves that it was possible for trained observers to assess degrees of " flattening " of affect in schizophrenics with reasonable agreement using a three-point scale—grossly flat affect, moderately flat affect, and normal affect—the authors proceeded to the first part of this study, in which the case records of 413 schizophrenic patients at the Bethlem Royal and Maudsley Hospitals, London, were examined. In 178 patients in whom flattening of affect was noted a significantly positive correlation was found between this factor and age, other severe psychotic features, and outcome, the prognosis being less favourable in this group than in the 235 patients without flattening of affect.

In the second part of the study 40 schizophrenic patients with gross psychotic features were taken at random. Their affect was estimated on the three-point scale and each was also given a battery of psychological tests, including a shortened version of the Wechsler Bellevue test, the Rampton Hospital Sorting test, the Nufferno Speed test, the Recognition of Absurdities test, and the series of Wegrocki's tests. Those patients with flattening of affect showed a poorer performance in those tests involving intellectual processes and did particularly badly in tests involving speed. The authors speculate that the flattening of affect may be due to the contrast between the patient's slowness and the observer's normality [but the cause of the slowness is not considered]. *L. G. Kiloh*

1120. **Organic Basis of Confusional States in the Elderly**
F. J. FLINT and S. M. RICHARDS. *British Medical Journal* [*Brit. med. J.*] **2**, 1537–1539, Dec. 29, 1956. 6 refs.

The aetiological factors causing mental confusion of recent onset in 242 elderly patients at Fir Vale Infirmary, Sheffield, are discussed. In 188 cases mental confusion was attributed to an organic lesion, which in 118 was extracerebral; in the remaining 54 cases no specific cause was found, but the information available was often incomplete. The mortality was 76% in the confused group, compared with 50% in a comparable group of elderly patients who were rational; this abnormally high mortality was in part explained by local factors. Of 82 cases in which the cause of the confusion was cerebral, 66 showed evidence of cerebral infarction; but in 21 cases of presumed recent infarction no focal signs were elicited. The authors point out that cerebral infarction, especially the massive type, is often associated with an increase in the protein content of the cerebrospinal fluid, hence the diagnostic value of lumbar puncture in doubtful cases. Frank cerebral haemorrhage was seen in only 7 cases. Heart failure caused the mental confusion in 53 cases, 39 patients being in congestive failure, and pulmonary diseases, especially bronchopneumonia and bronchitis, were the cause in 46. Uraemia was present in 26 patients; in 15 of the 21 males in this group it was due to prostatic hypertrophy. The real incidence of uraemia, true or pre-renal, was probably higher because the authors point out that the blood urea level was not always estimated.

Other aetiological factors in this large series were severe anaemia, hepatic failure, avitaminoses, diabetes mellitus, and thyroid disorders. The authors emphasize the susceptibility of the ageing brain to anoxaemia of whatever cause, and the dangers of trivial infections,

dehydration and ionic imbalance, and sedation in elderly people with diminished functional reserves.

[It is not clear how often the diagnosis of cerebral infarction was presumptive and how often it was based on necropsy findings.] *J. N. Agate*

TREATMENT

1121. **The Effect of Chlorpromazine on Hepatic Function and Morphology**
J. K. DeVore, C. Daugherty, and E. M. Schneider. *Gastroenterology* [*Gastroenterology*] **31**, 391–398, Oct., 1956. 2 figs., 18 refs.

The effect of chlorpromazine on hepatic function was studied in two groups of patients. The first group of 8 patients had received a large dosage of chlorpromazine —1,500 to 3,500 mg. daily for 183 days, but none showed any significant abnormalities. The second group of 4 patients had jaundice following chlorpromazine therapy, but the dosage of the drug had been much smaller than that given in the first group, 3 having received 150 mg. or less daily for 38 days and one having been treated for 7 days only [dosage not recorded]. In the second group there was a marked increase in the serum alkaline phosphatase level and a lesser increase in the serum lipid phosphorus level. "Plugging" of bile canaliculi was noted in 3 patients in the second group and some periportal lymphocytic infiltration in 2. The jaundice disappeared rapidly in all 4 cases, in spite of continued administration of chlorpromazine, but there was a consistent rise in the serum cholesterol ester level during convalescence. *A. Wynn Williams*

1122. **The Activity of a New Phenothiazine Derivative in Psychiatry and Neurology.** (Activité d'une nouvelle phénothiazine en psychiatrie et en neurologie)
J. Sigwald, M. Henne, D. Bouttier, C. Raymondeaud, and A. Quetin. *Presse médicale* [*Presse méd.*] **64**, 2011–2014, Dec. 1, 1956. 2 refs.

The acid maleate of L-methoxy-3-(dimethylamino-3-methyl-2-propyl)-10-phenothiazine ("7044 RP") is a new drug of therapeutic interest. Experimentally it has a sympathicolytic and parasympathicolytic activity inferior to that of chlorpromazine, but its spasmolytic activity is identical with that of chlorpromazine. Its antihistaminic activity is important, being superior to that of promethazine, and its psychomotor depressant action has been shown to be about 75% greater than that of chlorpromazine.

The therapeutic effects of the drug in a series of 51 patients suffering from various psychiatric disorders are reported in this paper. The results obtained were similar to those with chlorpromazine, 7044 RP being perhaps a little more active in a smaller dosage. The drug was effective in mania and various states of agitation, less constantly in melancholia, and least in severe states of neurotic depression. It was effective in various neurotic disorders (*les petits mentaux*). In hallucinatory and interpretative delirium its effect was comparable with that of chlorpromazine.

The drug was also found to be effective in certain neurological disorders, especially by reason of its action on pyramidal and extrapyramidal manifestations. It was particularly useful in the treatment of depressive forms of the Parkinsonian syndrome and in cases of severe pain such as that due to malignant metastases or herpes zoster in old people.

The same side-effects were noted with 7044 RP as with chlorpromazine, and included somnolence, postural hypotension, and tachycardia. In 2 cases transient urinary incontinence was caused, but in one case a cutaneous photosensitivity which had been provoked by chlorpromazine was found not to occur with 7044 RP.
J. MacD. Holmes

1123. **Trial of Reserpine in Treatment of Schizophrenia**
J. N. P. Moore and E. A. Martin. *British Medical Journal* [*Brit. med. J.*] **1**, 8–14, Jan. 5, 1957. 10 refs.

Reserpine given orally may benefit deteriorated chronic hospitalized schizophrenics with troublesome symptoms. Chronic schizophrenics who have failed to achieve a sustained remission following electric convulsion therapy (E.C.T.), insulin coma, or leucotomy may improve remarkably with intensive reserpine therapy. As a result of our experience we have made it a rule that no schizophrenic should be leucotomized without first having prolonged trial on reserpine. Patients with schizophrenia of insidious onset but without florid symptoms or gross personality deterioration may respond favourably to intensive reserpine therapy. It is probably necessary to continue on an oral maintenance dose for a prolonged period. Immediate results of reserpine therapy in acute schizophrenics are impressive. Observation over a prolonged period alone can determine whether in these early cases it is a better therapeutic agent than insulin coma therapy.

Severe depression of the endogenous type with characteristic early morning waking and suicidal preoccupation is the most serious complication of the treatment. The incidence of this complication was greatest in the schizo-affective type of psychosis. A past history of endogenous depression is a contraindication to the use of the drug. Some chronic schizophrenics improve on oral dosage only. Intensive and prolonged treatment seems necessary in most cases of progressive schizophrenia. Some patients with chronic anxiety states, especially if underweight, may benefit from oral reserpine. The results in most cases are not so dramatic as in schizophrenia. Most patients on reserpine eat better and put on weight. Cases of anorexia nervosa may improve rapidly on the drug.

The extensive use of reserpine alters the character of a psychiatric unit considerably. Negativistic, aggressive behaviour is greatly diminished. Patients can enjoy more freedom and take a more active part in the hospital routine. It places an increased demand on hospital staff for individual psychotherapy.—[Authors' summary.]

1124. **Comparison of Clinical Effects of Chlorpromazine and Reserpine in Psychotic Patients**
D. Goldman. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 137–144, Feb., 1957. 3 refs.

Dermatology

1125. **Venous Lakes**
W. B. BEAN and J. R. WALSH. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **74**, 459–463, Nov., 1956. 7 figs., 10 refs.

Under the name of "venous lakes" the authors describe a type of lesion which is common but unobtrusive, and apparently has not been reported previously. Venous lakes are thin-walled superficial structures resembling at first glance simple traumatic blood blisters, but less tense and with some irregularity of the elevated surface. They are dark blue in colour, and the blood can be expressed with the finger, refilling occurring slowly. Varying in size from 1 to 5 mm. they are most commonly found on the ears, face, and lips of men in later life. Their wall contains very little muscle tissue and they are probably dilated rather than overgrown or hypertrophied venous structures. Ageing and minor injury are thought to be the chief aetiological factors. They cause no symptoms unless traumatized, as in shaving, when bleeding is persistent. [Treatment is not discussed.] *S. T. Anning*

1126. **Eccrine Poroma. Tumors Exhibiting Features of the Epidermal Sweat Duct Unit**
H. PINKUS, J. R. ROGIN, and P. GOLDMAN. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **74**, 511–521, Nov., 1956. 5 figs., 16 refs.

The histology of the epidermal sweat-duct unit or acrosyringium is described and the features to be expected in a tumour of this structure are discussed. Five examples of tumours with these characteristics are reported from Detroit Receiving Hospital and the Sinai Hospital of Detroit, all being small, benign new growths resembling papilloma or granuloma pyogenicum and occurring on the non-hairy surfaces of the foot. Histologically, while the structure resembled that of the seborrhoeic wart and basal-cell epithelioma, it showed features suggesting that the tumour was related structurally to the epidermal eccrine sweat-duct unit, and the name "eccrine poroma" is proposed for this subgroup of the hidradenomata. *S. T. Anning*

1127. **Treatment of Cutaneous Fungus Infections with a Phenylsalicylamide Derivative**
F. KEDDIE, G. F. HEXTER, and A. S. BROWN. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **74**, 504–510, Nov., 1956. 5 refs.

This paper reports a clinical trial in various fungus infections of the skin of a new fungicide, "bynamid" (N-*n*-butyl-β-phenylsalicylamide), which was used in the form of a tincture (5 or 15%), an ointment (5%), a lotion (5%), and a powder (5%). [The formulae are given.] There were 159 patients (with 222 infected sites), 36 of whom were infected with *Trichophyton rubrum*, 28 with *Candida albicans*, and 25 with *T. mentagrophytes*, other fungi accounting for 28 infections, while in 42 cases the organism was not identified. In all, 32% of the lesions disappeared, 45% improved, and 23% showed no change. Of infections involving the trunk, arms, legs, and crura, 47% were cleared. Of those involving the hands, feet, and nails, 21% were cleared. Recurrences responded readily to further treatment. These cure rates were similar to those in a series of patients treated with undecylenic acid. It is, however, noteworthy that, of 40 patients with infected nails, 7 were cured. The incidence of irritation was low.
S. T. Anning

1128. **Acne Vulgaris**
R. M. B. MACKENNA. *Lancet* [*Lancet*] **1**, 169–177, Jan. 26, 1957. Bibliography.

1129. **Toxic Epidermal Necrolysis; an Eruption Resembling Scalding of the Skin**
A. LYELL. *British Journal of Dermatology* [*Brit. J. Derm.*] **68**, 355–361, Nov., 1956. 5 figs., 1 ref.

A syndrome characterized by widespread or total shedding of the epidermis is described in this paper from the Royal Infirmary, Aberdeen. The loosening of the skin had been preceded by erythema and tenderness and was followed by peeling, so that a dark red, excessively tender surface was revealed which healed rapidly without scar formation. All 4 patients looked as though they had been scalded, but the shock that such extensive injury would produce was absent. In one case as much as 80% of the skin was involved. The condition appeared to be a toxic epidermal necrolysis; in 2 cases drug toxicity was suspected. The author points out that in this condition, which differs from erythema multiforme, pemphigoid, and pemphigus, areas of epidermis are lifted from the dermis by acellular fluid. He considers that the term toxic epidermal necrolysis serves to distinguish the condition from other toxic erythemata and bullous eruptions, and avoids the ambiguity of epidermolysis and the picture of ulceration and gangrene which is suggested by the word necrosis.
G. B. Mitchell-Heggs

1130. **Studies on the Local Effect of Various Cortisone Preparations on Experimentally Produced Eczematous Reactions.** [In English]
H. HAXTHAUSEN. *Acta dermato-venereologica* [*Acta derm.-venereol. (Stockh.)*] **36**, 381–388, 1956. 3 figs., 8 refs.

1131. **Lichen Planus Treated with Grenz Rays. (Preliminary Report.)** [In English]
H. KOPP and F. E. REYMANN. *Acta dermato-venereologica* [*Acta derm.-venereol. (Stockh.)*] **36**, 477–481, 1956. 3 figs.

Paediatrics

1132. **A Controlled Study of the Use of Prophylactic Antimicrobials in Premature Infants. Bacteriologic Observations**
G. GIALDRONI-GRASSI, C. V. PRYLES, and M. FINLAND. *Pediatrics* [*Pediatrics*] **18**, 899–916, Dec., 1956. 1 fig., 25 refs.

At Boston City Hospital (Harvard Medical School) nose and throat swabs were taken from 49 premature infants within a few hours of birth; 90% of the nasal cultures and 80% of the throat cultures were sterile. Thereafter the infants were divided into four groups: the first received penicillin and streptomycin, 25,000 units and 40 mg. per kg. body weight daily respectively; the second received sodium sulphadiazine, 125 mg. per kg. daily; and the third oxytetracycline, 25 mg. per kg. daily. The fourth group served as a control. The prophylactic therapy was given 12-hourly by intramuscular injection and was continued for 10 days. Further swabs were cultured on the 3rd, 5th, and 10th days and, in 34 cases, on the 30th day also.

The development of the bacterial flora was similar to that reported by previous workers, staphylococci appearing first—both in the nose and the throat—and *Streptococcus viridans* following—predominantly in the throat. The resistance of the organisms also followed the expected pattern, the staphylococci being resistant and the streptococci sensitive to all the agents used.

The prophylactic therapy appeared to have little effect on the bacteriological findings, except that enterococci tended to replace the normal flora during the period of treatment with sulphadiazine and oxytetracycline. In the cultures taken on the 30th day there was little difference between the flora obtained from the 16 infants still in hospital and that from the 18 infants who had been home for a week or more. *Wilfrid Gaisford*

1133. **Hypocalcemia Occurring on the First Day of Life in Mature and Premature Infants**
I. F. GITTLEMAN, J. B. PINCUS, E. SCHMERZLER, and M. SAITO. *Pediatrics* [*Pediatrics*] **18**, 721–729, Nov., 1956. 34 refs.

The authors studied the incidence of hypocalcaemia on the first day of life in 1,019 infants born in New York City. No details of symptoms or signs are recorded, but for the purposes of this investigation hypocalcaemia was considered to be present when the blood calcium level fell below 8 mg. per 100 ml. in venous blood in the case of full-term infants and in capillary blood in that of premature infants, a study in 14 mature infants on the first day of life having indicated that the calcium levels in venous and capillary blood were comparable.

Pregnancy and delivery were normal for 824 of the births, and 10 (1·2%) of the infants developed hypocalcaemia; all 14 infants born per vias naturales after an abnormal pregnancy had hypocalcaemia. Caesarean section was performed for disproportion in 51 cases and 7 of the infants had hypocalcaemia; it was also performed in 19 cases because of placenta praevia, diabetes, or toxaemia, and 7 of these infants had hypocalcaemia. Of 111 premature infants, hypocalcaemia was present in 32 out of 66 born after a normal pregnancy and labour, in 18 out of 36 born after an abnormal pregnancy and labour [cause not stated], in one of 2 infants delivered by Caesarean section because of " repeat sections " in the mother, and in 4 out of 7 delivered by Caesarean section after an abnormal pregnancy. There was a significant positive correlation between the weight of the premature infant and the blood calcium level.

The causes of hypocalcaemia are discussed with special reference to abnormal pregnancy, renal function, and blood corticosteroid levels. The incidence of hypocalcaemia is higher in infants born after an abnormal pregnancy, whether delivery is per vaginam or by Caesarean section, than in those born after a normal pregnancy, and it is suggested that this may be due to the effect of abnormal pregnancy upon renal function in the foetus and the newborn—reduced glomerular filtration, poor urea clearance, and increased urinary excretion of phosphate. Adrenocorticosteroids depress the serum calcium level, and the authors suggest that hypocalcaemia in the newborn is the result of increased production of adrenocorticosteroids during the last trimester of pregnancy [but in this study no adrenocorticosteroid levels were determined in support, or otherwise, of this suggestion.] *R. M. Todd*

1134. **Erythrocyte Production and Iron Stores in Premature Infants during the First Months of Life. The Anemia of Prematurity—Etiology, Pathogenesis, Iron Requirement.** [In English]
M. SEIP and S. HALVORSEN. *Acta pædiatrica* [*Acta pædiat. (Uppsala)*] **45**, 600–617, Nov., 1956. 7 figs., 27 refs.

In order to elucidate the aetiological and pathogenetic factors in the anaemia of premature infants and also their iron requirements, 16 such infants weighing less than 2,000 g. at birth were studied at the Children's Hospital, Oslo. As an estimate of erythrocyte production reticulocyte counts were performed twice a week, and iron stores were determined in samples of bone marrow removed between the 3rd and 5th days of life and at 4-weekly intervals thereafter (90 such preparations were examined from 118 bone-marrow punctures); haemoglobin levels were determined weekly, and the rate of growth was estimated by expressing the weekly weight gain as a percentage of the weight recorded at the beginning of the week.

From their findings the authors contend, in contrast to other workers, that the intensive growth of these infants is probably the most important pathogenetic

factor in the anaemia of prematurity, together with the added factor of increased haemolysis owing to the shorter life span of foetal erythrocytes. The intensity of growth leads to an increase in blood volume, with subsequent blood dilution and a fall in the haemoglobin level, which stimulates the bone marrow; this response is due to the increased oxygen consumption arising from the intensive growth. The inability of the blood-producing organs to meet these demands is also a factor in the anaemia of prematurity. Studies of the iron stores showed a rapid increase in haemosiderin (after its initial absence at birth), there being a steady increase reaching a maximum between 4 and 8 weeks followed by a steady decrease till at about 12 weeks none was present; there was less haemosiderin, and it disappeared earlier, in the smaller premature infants. The controversial point of when best to give iron to premature infants is discussed. From the results of the reticulocyte counts and the iron-deposit studies the authors conclude that in order to safeguard against anaemia iron should be given before the haemosiderin deposits begin to decrease, namely, at 4 to 6 weeks for the smaller premature infants and at 6 to 8 weeks for the heavier infants.

David Morris

1135. **Mean Venous Pressures in the First Hours of Life**
R. E. Bonham-Carter, J. P. Bound, and J. M. Smellie. *Lancet* [*Lancet*] **2**, 1320–1323, Dec. 29, 1956. 6 figs., 6 refs.

At University College Hospital, London, the authors have measured the mean venous pressure during the first hours after birth in normal babies, in babies with the pulmonary syndrome of the newborn (hyaline membrane, pulmonary oedema and haemorrhage, and resorption atelectasis), and in babies with cerebral irritation. A polythene catheter of 1-mm. bore filled with 5% dextrose solution containing 500 units of heparin per 100 ml. and attached to a manometer was passed 5 to 8·5 cm. up the umbilical vein until the meniscus in the manometer rose and fell freely with respiration and this level was recorded, a zero level corresponding to the level of the sternal angle being indicated by a sliding pointer. The box containing the baby was then tilted feet downwards to an angle of 45 degrees and further readings were taken, the baby being returned to the horizontal position for a final reading. Most of the records were made during the first 24 hours of life and the babies were usually quiet at the time.

Five groups were studied. (1) In 35 healthy babies of birth weight 2½ to 9 lb. (1·13 to 4·07 kg.) the venous pressure averaged +2·6 cm. of 5% dextrose solution and in 95% fell within the range +0·2 to +5·0 cm. in the supine position. The mean pressure in 15 cases after tipping feet down was −2·0 cm., with a mean fall of 4·9 cm. Birth weight and age up to 18 hours after birth did not influence the readings obtained. (2) Of 12 babies requiring resuscitation at birth but appearing normal at the time of measurement, only one had a venous pressure above the normal range. In the 7 babies who were tipped the mean venous pressure was +0·7 cm. (mean fall 4·7 cm.). (3) Of 32 babies with respiratory difficulty, 25 were examined within the first 6 hours after birth. Of these, 17 who survived had a mean pressure of +5·7 cm., which is significantly higher than normal, whereas 8 who died had a mean pressure of +3·1 cm., which is significantly lower than that of the survivors. Of the 7 others who were examined later, all of whom survived, all but 2 had a venous pressure within the normal range. (4) Of 8 babies with cerebral irritation the venous pressure in 3 was above +5·0 cm. and in the remainder within normal limits. (5) In 4 out of 5 infants with erythroblastosis foetalis who survived the venous pressure was raised before exchange transfusion but fell after successful treatment. In the fifth case the pressure was normal before exchange transfusion, but the baby died and hyaline membrane was found at necropsy.

In the 6 abnormal babies with increased venous pressure who were tipped the mean fall in pressure was 6·5 cm., and in the 14 with normal pressure it was 5·2 cm., whereas in the normal babies the mean fall was 4·9 cm. A raised venous pressure in ill babies was associated with survival, while in all fatal cases (and in premature babies) the pressure was within the normal range.

[This work is useful as a further step in unravelling the abnormal physiological processes which may be present in the newborn.] *Pamela Aylett*

1136. **Generalized Cytomegalic Inclusion Disease in Newborn Infants**
M. Birdsong, D. E. Smith, F. N. Mitchell, and J. H. Corey. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 1305–1308, Dec. 1, 1956. 3 figs., 8 refs.

CLINICAL PAEDIATRICS

1137. **Essential Hypertension in Infancy and Childhood. Differential Diagnosis and Therapy**
R. J. Haggerty, M. W. Maroney, and A. S. Nadas. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **92**, 535–549, Dec., 1956. 4 figs., 49 refs.

A persistent systolic blood pressure of 130 mm. Hg and a diastolic pressure of 90 mm. Hg in the absence of any defined cause is accepted by the authors as diagnostic of essential hypertension in childhood. At the Children's Medical Center, Boston, 9 such patients below the age of 14 years, seen during a 15-year period, have been studied; in 5 of these cases the hypertension was severe (160/110 mm. Hg or above). The literature of the condition is reviewed and the differential diagnosis and treatment discussed.

Cardiovascular complications were found only in the 5 children with severe hypertension, and while in these a family history of hypertension was uncommon, all the patients mildly affected gave such a family history. In the differential diagnosis the rarity of this condition in children should be borne in mind and an exhaustive search made for some cause of the increased blood pressure, particular attention being paid to the possibility of unilateral renal disease. The pharmacological application of some of the antihypertensive drugs is considered;

in the authors' experience most success in the group with encephalopathy was obtained with trimethaphan camphorsulphonate ("arfonad"). Other therapeutic measures, such as sedation, weight reduction, psychotherapy, a low-sodium diet, and adrenalectomy are considered, and the irregular results obtained with sympathectomy are noted. Because of the variable response of these patients to different forms of treatment no uniform regimen has been possible, the management of each patient being determined by his individual response to the therapeutic measures employed.

I. A. B. Cathie

1138. **Giant Cell Pneumonia. Clinico-pathologic and Experimental Studies**
J. M. ADAMS, D. T. IMAGAWA, M. YOSHIMORI, and R. W. HUNTINGTON. *Pediatrics* [*Pediatrics*] **18**, 888–898, Dec., 1956. 3 figs., 24 refs.

The authors report 4 cases of giant-cell pneumonia, one in a child aged 5½ years and 3 in infants 3 weeks to 9 months of age. Two were directly associated with measles, and death was due to acute interstitial giant-cell pneumonia; in the other two there were similar necropsy findings and the suggested diagnosis was "primary pneumonitis with inclusion bodies". There were no characteristic distinguishing clinical features in any of the cases.

After inoculating ferrets with two types of canine distemper virus and with adenoviruses from human tonsil and adenoid tissues the authors succeeded in demonstrating inclusion bodies and giant cells in various tissues, provided the animals lived for at least 13 days. They conclude that the development of giant cells depends on the duration of the lung infection and may occur as a result of infection by any of a large number of viruses.

Wilfrid Gaisford

1139. **Drug Treatment of Enuresis. Controlled Trials with Propantheline, Amphetamine, and Pituitary Snuff**
K. S. HOLT. *Lancet* [*Lancet*] **2**, 1334–1336, Dec. 29, 1956. 8 refs.

Stating that "about half a million English schoolchildren are said to wet their beds regularly" the author describes a controlled trial of propantheline, amphetamine, and pituitary snuff in the out-patient treatment of nocturnal enuresis in 88 children at Sheffield Children's Hospital. The children ranged in age from 4 to 14 years and all of them had only an occasional dry night. Only those with no symptoms or signs suggestive of organic lesion of the urinary tract were included in the trial. Advice concerning general management was offered and a chart for recording wet and dry nights to be kept by the patient or parent was provided, together with a supply of a drug or placebo preparation which was allocated according to a random system and was sufficient for a 4-week period. For the next 4 weeks those previously given a drug received the placebo, and vice versa.

Of propantheline (which was chosen for its anticholinergic action) 60 mg. was given at bedtime. Amphetamine was given to lighten the depth of sleep, 10 mg. or in some cases 20 mg. of the sulphate being taken before going to bed. The posterior-pituitary snuff ("di-sipidin") was given as one or two capsules (30 or 60 antidiuretic units), the contents of which were introduced into the nose by means of a simple insufflator which most of the children could use themselves. For each drug the corresponding placebo was of similar appearance. A total of 171 trials on the 88 patients were carried out; the results are tabulated.

Of the 43 children receiving the placebo first, 16 (37%) reported improvement, 10 having between 15 and 21 dry nights out of the 28. In some trials the drug gave better results than the placebo, in others not. Thus 60 mg. of propantheline was not more effective than the placebo and 7 of the 40 children receiving this drug had side-effects such as abdominal pain, nausea, vomiting, and blurred vision. Of the 49 children given amphetamine sulphate, 8 improved, but 5 of these were wakeful at night and tired in the daytime, and side-effects in the form of restlessness, abdominal pain, or nervousness occurred in 17. Lastly, of 60 children given posterior-pituitary snuff, 8 showed marked improvement and no side-effects were observed.

[This study shows that inert tablets may have a considerable influence upon enuresis, but the problem of nocturnal enuresis as a whole remains unsolved.]

Pamela Aylett

1140. **The Schönlein–Henoch Syndrome with Particular Reference to Renal Sequelae**
R. J. DERHAM and M. M. ROGERSON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 364–368, Oct., 1956. 10 refs.

The authors present a follow-up report on 17 out of 35 cases of the Schönlein–Henoch syndrome seen between 1943 and 1950 and previously described (*Arch. Dis. Child.*, 1952, **27**, 139), together with an analysis of the clinical findings in a further 59 cases admitted to Alder Hey Children's Hospital, Liverpool, between 1951 and 1955. The earlier cases were reviewed with the object of determining the incidence and prognosis of renal complications, since the role played by the Schönlein–Henoch syndrome in the aetiology of nephritis is still uncertain. Of the original 35 patients, 19 had had some degree of renal involvement while in hospital and in 4 albumin and erythrocytes were still present in the urine at the time of discharge; of these last, 3 are now quite well but the fourth suffered from albuminuria for 8 years.

It was possible to trace 17 patients of the early series and of these, 9 had had no recurrence of symptoms, 5 had occasional pain and swelling of the joints, 2 showed mild or moderate impairment of renal function, and one severe renal deficit; in this last case, in a girl of 15, the situation was complicated by a recent nephrectomy for hydronephrosis. Of the 59 cases in the present series (nearly half in patients aged between 5 and 7 years), 27 had renal involvement of varying degree during their first admission and 2 died of "chronic nephritis", though one had no renal complication until 9 weeks before his death from uraemia. Ten of the 59 patients were readmitted to hospital, 9 within 4 months of dis-

charge and one after 2 years; of these, 4 had purpura, 7 developed haematuria, and 4 now have chronic nephritis. The main clinical findings in the whole series of patients and in 4 atypical cases are reviewed; 2 children who had no evidence of renal damage initially now show moderate renal impairment. Chorea was an associated complication in 2 cases.

In spite of these findings the authors contend that the renal manifestations in this condition represent "renal bleeding" rather than true nephritis.

Margaret D. Baber

1141. **Neurological Complications in the Schönlein–Henoch Syndrome**

I. C. Lewis and M. G. Philpott. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 369–371, Oct., 1956. 10 refs.

In view of the rarity, as judged by the paucity of reports in the literature, of serious neurological complications in patients with the Schönlein–Henoch syndrome the authors record 3 cases (diagnosed by Gairdner's criteria) in children, 2 of whom developed a subarachnoid haemorrhage and one hypertensive encephalopathy. The first child, aged 8, had a convulsion, presumably hypertensive, followed by subarachnoid haemorrhage, before any evidence of renal damage was found, and later he developed a hemiplegia presumably due to cerebral haemorrhage or thrombosis. The second patient, a girl aged 10, was found to have abnormal urine only 2 days after subarachnoid haemorrhage was diagnosed. The cerebral symptoms cleared rapidly, but her renal condition deteriorated steadily, the urine being loaded with albumin, and she died 4 months later; the clinical and post-mortem findings were those of subacute nephritis. The third child, a girl aged 6, had periods of confusion or unconsciousness and occasional convulsions associated with hypertension (up to 145/120 mm. Hg), but no evidence at any time of renal damage. This patient made a good recovery and the urine remained normal throughout. [The cerebrospinal fluid was not examined.]

It is suggested that arteriolitis of the cerebral vessels may be the cause of the neurological complications in this syndrome. Cortisone was administered in the first case and prednisone in the third, but without benefit.

Margaret D. Baber

1142. **Carcinoma of the Thyroid in Children. A Report of Ten Cases**

G. H. Fetterman. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **92**, 581–587, Dec., 1956. 6 figs., 13 refs.

The author, writing from the Children's Hospital of Pittsburgh, reports 10 further cases of carcinoma of the thyroid in children, 9 of which have been seen in the past 6 years. Metastases were present in 9 of the 10 cases and the wide range of treatment employed, which is described, has led to the survival of all the patients so far, the period of follow-up being 3 months to 8 years. The importance of dealing very seriously with all nodules in the thyroid gland in children is stressed. No fewer than 8 of these children had had irradiation to the face, neck, or chest from 3 to 12 years before the diagnosis of thyroid carcinoma. The question is discussed whether the incidence of thyroid carcinoma is on the increase and, as a corollary, whether such an increase is due to irradiation in infancy. In the author's opinion, until more information is available, the use of ionizing radiations in infancy should be reduced to the minimum.

I. A. B. Cathie

1143. **Nodular Lesions of the Thyroid Gland in Children**

A. B. Hayles, R. L. J. Kennedy, L. B. Woolner, and B. M. Black. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **16**, 1580–1594, Dec., 1956. 5 figs., 10 refs.

A review of the records has shown that nodular enlargement of the thyroid gland was found in 130 children aged 14 years or younger examined at the Mayo Clinic during the years 1908 to 1955. The cause of the nodular enlargement was lymphocytic (Hashimoto's) thyroiditis in 8 patients, goitrous cretinism in 5, and congenital goitre in 3, but benign adenoma (68 cases) and carcinoma (46) were the cause in over 80% of the cases.

Patients suffering from benign adenoma were usually euthyroid. In about one-third of the 68 cases the adenoma was single; the weights of the adenomata varied widely, from single tiny nodules to one massive goitre consisting of multiple adenomata weighing 250 g. Enlargement of the cervical lymph nodes was the presenting complaint in 36 of the 46 patients with carcinoma; in 41 of these cases the histological appearance was of papillary and follicular adenocarcinoma. During the years covered by the survey the incidence of benign adenoma has declined, possibly owing to the widespread use of iodized salt. On the other hand the incidence of carcinoma has risen steadily, from 4·5% of all nodular goitres during the years 1908 to 1919 to 70% during the period 1950–5; the authors suggest that this increased incidence may be related to the increase in treatment with *x*-ray irradiation. They stress that the figures given above do not represent the true incidence of nodular goitre in children, since two-thirds of the patients were referred to the Clinic after diagnosis of carcinoma of the thyroid elsewhere.

R. M. Todd

1144. **Hip Dislocation in Cerebral Palsy**

M. O. Tachdjian and W. L. Minear. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **38-A**, 1358–1364, Dec., 1956. 17 refs.

Of 590 patients with cerebral palsy, seen at the Carrie Tingley Hospital for Crippled Children, Truth or Consequences, New Mexico, 25 (4·24%) showed evidence of dislocation or subluxation of the hip. Radiographs in 20 of the 25 patients disclosed an average coxa valga of 170 degrees, with a maximum of 178 and a minimum of 160 degrees. In 6 patients with 7 affected hips the acetabular index was over 25 degrees. The sex and age incidence, ability to bear weight, and the type of cerebral palsy are discussed; 23 of the 25 patients had spastic cerebral palsy. The dynamic imbalance of the muscles about the affected hip was studied in repeated composite

muscle tests. The authors point out that in examining the muscles of a child with cerebral palsy tension athetosis should be distinguished from spasticity. Tension athetosis is produced by the intentional effort of the athetoid patient to prevent any undesired movement of the limb. Voluntary tension can be recognized by shaking the limb, when the tension can be lessened. The spastic limb, however, resists shaking, the spastic position being maintained.

The treatment of these patients and the end-results are discussed, the importance of prophylactic tenotomy of the spastic hip adductors and of strengthening the motor power of the abductors being emphasized. The authors state in conclusion that dislocation of the hip in cerebral palsy is preventable. "If we are aware of the probabilities and understand the pathomechanics, every child with spastic lower limbs will be regarded as in danger of having either subluxation or dislocation of the hip." *Leon Gillis*

1145. **The Diagnosis of Cerebral Phlebitis in Children. Value of Extracranial Venous Signs.** (Le diagnostic des phlébites cérébrales chez l'enfant. Valeur des signes veineux extracraniens)
M. BERNHEIM and F. LARBRE. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **13**, 1021–1042, 1956. 5 figs., 6 refs.

From the Hôpital Edouard-Herriot, Lyons, the authors describe their experience in 15 cases of cerebral phlebitis in children, with special reference to diagnosis. Clinically the syndrome may present in three different forms. (1) Superacute cases, starting suddenly with convulsions, coma, and hyperthermia and progressing rapidly to death; of the 4 cases in this group, 2 are described in detail, including the post-mortem findings. (2) Cases also characterized by sudden onset of fever, convulsions, and coma, but in this type the convulsions tend to be focal and recovery soon sets in, although there are usually permanent sequelae in the form of hemiplegia or mental deterioration; of the authors' 3 cases of this type, the clinical details of one are presented. (3) In the third type (8 cases) the initial signs and symptoms are the same as in the other groups, but here the patients recovered completely and left the hospital without any signs of permanent neurological damage. The aetiology of the cerebral phlebitis could not be established with certainty in every case. Aural or mastoid suppuration or cutaneous infection of the face or scalp seemed to be the most frequent causes.

The clinical diagnosis depends upon the recognition of the sudden onset of convulsions accompanied by high fever and localizing neurological signs, or (as occurred in 3 of the present cases) there may be signs of intracranial hypertension without evidence of neurological localization. The discovery of infection of the ears, upper respiratory passages, or the skin, the presence of prominent scalp veins and oedema of the tissues, together with leucocytosis and changes in the cerebrospinal fluid suggestive of meningeal reaction, assist greatly in diagnosis. The particular superficial veins which are thrombosed are often a guide to which sinus is the site of the phlebitis. Changes in the electroencephalogram may also be of additional diagnostic value, and some characteristic records in the series are described in the text.

In discussing the treatment the authors lay particular stress on the early use of anticoagulants (particularly heparin) in addition to vigorous administration of antibiotics. *Marcel Malden*

1146. **The Diagnosis, Treatment, and Prognosis of Tumors Affecting the Spinal Cord in Children**
F. C. GRANT and G. M. AUSTIN. *Journal of Neurosurgery* [*J. Neurosurg.*] **13**, 535–545, Nov., 1956. 4 figs., 2 refs.

The authors present a brief review of a series of 30 cases of tumour of the spinal cord in patients under the age of 15 years. Diagnosis is discussed with particular reference to myelography. In 12 cases the tumour was extradural, in 12 intradural, and in the remaining 6 it was intramedullary. The histological diagnoses of the various types of tumour are listed. The operative mortality was 6·7%; 18 (60%) of the tumours were benign and 9 of the patients (30%) were alive and well 10 years after the operation. *L. Crome*

1147. **Clinical Features of Children Suffering from Neurological Sequelae of Rh Iso-sensitization**
C. BURTON-BRADLEY. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **5**, 203–213, Aug. [received Nov.], 1956. 2 figs., 15 refs.

The author reports the results of a study carried out at the Spastic Centre, Mosman, New South Wales, on a group of 18 children who suffered from neurological lesions after recovery from icterus gravis neonatorum. In most cases blood transfusions varying in number from one to five had been given. The ages of the patients at the time of examination ranged from 8 months to 8 years. In the early days of life some of the affected children in this series had shown varying degrees of opisthotonus, but later there was apparently complete recovery of function and feeding was usually established normally.

The first sign of a permanent neurological defect was a persisting delay in either walking or speaking. When the ability to walk was acquired it was accompanied by a disturbance of gait (the "toe–heel" gait), which the author regards as highly characteristic of these patients; it is similar to that seen in children with athetosis, which was present in 17 of the 18 children. Among other neurological abnormalities encountered was a defect of ocular movements most commonly affecting upward movement of the eyes. Also frequently noted was deafness to tones of high frequency, and the author stresses the importance of recognizing this handicap which, together with the dysarthria associated with the athetosis, is an additional difficulty in the education of these children. The author also notes the presence of hypoplasia of the enamel of the deciduous teeth, causing the characteristic "Rh hump" at the gum line in 17 of the patients. Two detailed case histories are presented.
Fergus R. Ferguson

Medical Genetics

1148. **Genetic Aspects of Cystinosis (Cystine Storage Disease) and Its Relationship to Cystinuria and Hyperamino-aciduria.** (Zur Genetik der Cystinose (Cystinspeicherkrankheit) und ihre Beziehungen zur Cystinurie und Hyperaminoacidurie)
U. PFÄNDLER and H. BERGER. *Annales paediatrici* [*Ann. paediat. (Basel)*] **187**, 1–41, July–Aug., 1956. 48 refs.

The authors present, from the University of Berne and the University Children's Clinic, Basle, a genetic analysis of two Swiss families in which there was evidence of disturbances of amino-acid excretion. In the first family the propositi were 2 children, a boy and his sister, who died at the age of 3 and 2 respectively from cystinosis. In the second family the propositus was a boy who died at the age of one year with cystinosis.

In both families relatives of the first, second, and in some cases of the third degree were investigated, the urine being examined for excretion of cystine (by the Brand test), calcium (the Sulkowitsch test), and for total α-amino nitrogen (by the method of Antener), and by paper chromatography for the presence of individual amino-acids. Of the 49 members of the two families examined 19 were considered to have hyperamino-aciduria, 16 cystinuria, and 13 hypercalciuria. Some relatives were excreting abnormal amounts of individual amino-acids other than cystine, as estimated by the intensity of the individual " spots " on the chromatogram, particularly glycine, arginine, lysine, and α-alanine.

The hypothesis is put forward that many members of such families who are heterozygous for the gene which in the homozygous state causes cystinosis have hyperamino-aciduria, and that this abnormality may be complete or partial, with or without cystinuria. The literature is reviewed, with special reference to the work of Dent and Harris. *C. O. Carter*

1149. **The Inheritance of Muscular Dystrophy: Further Observations**
J. N. WALTON. *Annals of Human Genetics* [*Ann. hum. Genet.*] **21**, 40–58, July, 1956. 4 refs.

The results are reported of a survey of the mode of inheritance of muscular dystrophy as determined from a series of 67 cases occurring in 17 families. In 7 families containing cases of the Duchenne-type muscular dystrophy there were 37 cases of which one appears to be female, although her polymorphonuclear leucocytes do not show female characteristics. Nevertheless in all families the mode of inheritance was characteristic of that due to a sex-linked recessive gene. In 3 of the families the onset of the disease was as late as the second or third decade. In 3 families of facioscapulohumeral dystrophy there were at least 11 affected individuals including 3 abortive cases. The pattern of inheritance suggested that this disease is carried as an autosomal dominant character, though possibly with sex limitation (to females) or incomplete manifestation in some families. Nineteen cases of limb-girdle dystrophy occurred in 8 sibships of 7 families; this form of the disease appears to be transmitted as an autosomal recessive character. —[Author's summary.]

1150. **ABO Blood Groups and Secretor Character in Duodenal Ulcer. Population and Sibship Studies**
C. A. CLARKE, J. W. EDWARDS, D. R. W. HADDOCK, A. W. HOWEL-EVANS, R. B. MCCONNELL, and P. M. SHEPPARD. *British Medical Journal* [*Brit. med. J.*] **2**, 725–731, Sept. 29, 1956. 25 refs.

Recent work has suggested an association between blood group O and duodenal ulcer in several areas of Europe and in the U.S.A. The finding has been obtained by comparing the blood groups of ulcer patients with a control series of unaffected people living in the same area. Such controls can be unsatisfactory in that a population of mixed origin may contain elements with a high frequency both of group O and of duodenal ulcer without the two being causally connected. Sibship studies where the unaffected sibs act as controls are not subject to this criticism.

Data are presented for 293 duodenal ulcer sibships. An analysis of these gives no evidence to support the hypothesis that a group O individual is more likely to have a duodenal ulcer than are his A, B, or AB sibs. This result could be regarded as evidence in support of the suggestion that the previously found association was due to racial stratification within the populations concerned. There are, however, considerable objections to this explanation, and an alternative, that the findings are due to a maternal effect, is discussed.

The ability to secrete ABO blood group antigens in body fluids is an inherited character, and it seemed possible that secretors and non-secretors might have different susceptibilities to duodenal ulcer. We have therefore investigated the secretor character in the saliva of 514 unrelated duodenal ulcer patients and compared the results with those of 491 controls from the general population.

This analysis shows that there is a significantly higher proportion of non-secretors in the duodenal ulcer patients (35·0%) than in the controls (24·2%). This difference is found in both males and females of each of the ABO blood groups and in both macroscopically and radiologically diagnosed cases. These data suggest that non-secretor individuals may be about 45% more likely to develop duodenal ulcer than are secretors.

For the same reason as in the association between group O and duodenal ulcer, sibship studies have been carried out, and the results in 262 families suggest that the relationship between non-secretion and duodenal ulcer may hold within families.

The possibility that the ABO and Lewis antigens may confer some protection against duodenal ulceration by virtue of their mucoid character is discussed.—[Authors' summary.]

Public Health and Industrial Medicine

1151. **Epidemic of Pulmonary Tuberculosis in a Closed Community**
C. PROTHEROE. *British Medical Journal* [*Brit. med. J.*] 1, 80–82, Jan. 12, 1957. 1 fig.

The author reports on an outbreak of pulmonary tuberculosis among some members of a military band, who tended to live as a closed community of about 40 persons, having little in common with other members of their regiment. A bandsman who had recently joined this band had fallen ill with a pleural effusion, and a scanty distribution of tubercle bacilli was found in the concentrated fluid. He had come into close contact only with the other members of the band and with the bandmaster's family. An *x*-ray examination revealed pulmonary tuberculosis in 2 other cases, namely, a member of the band who had an advanced fibro-caseous lesion with cavities (and who, according to the author, had to be considered responsible for the spread of infection), and the bandmaster's wife who had an early infiltrative process. In the course of one year repeated radiological investigations were performed and 8 other cases of some form of pulmonary tuberculosis were discovered.

As the members of a military band play about 6 hours daily 5 days a week, often in a small practice room, droplet infection is presumably the chief route of spread of disease amongst them. A bandsman with open tuberculosis is exhaling much more air and with greater force than the average infected person, keeping the droplets airborne longer. As preventive measures in such a community the author suggests Mantoux testing of all persons under 21 years and B.C.G. inoculation of negative reactors, frequent radiological control, and routine chest *x*-ray examination of all bandsmen who suffer from any respiratory infection. Supervision by public health authorities, military or civilian, of the cleanliness of practice rooms, which should be large, light, and well ventilated, is essential. The mouthpieces of instruments should never be interchanged and should be disinfected regularly. *Franz Heimann*

1152. **A New Structure for Rural Health Services in the U.S.S.R.** (Новая структура сельского здравоохранения)
O. L. TREMBA. *Советское Здравоохранение* [*Sovetsk. Zdravookh.*] 14–17, No. 6, Nov.–Dec., 1956. 2 figs.

From April 1, 1956, the old system whereby hygiene and epidemiological work in the rural areas of the U.S.S.R. proceeded independently through scattered hygiene and epidemiological offices was replaced by a new system in which all branches of medicine—therapeutic, prophylactic, sanitational, and epidemiological—were brought under the unified control of a Chief Regional Medical Officer, working from the Central Regional Hospital, with three Deputies for hygiene and epidemiology, therapeutics and prophylaxis, and administration respectively. The advantages claimed are that the qualified medical personnel of each district have now become consciously responsible for the local hygiene, hitherto to a considerable extent in the hands of unqualified personnel; that there has been administrative saving as a result of the unification and the abolition of separate health stations; that the Deputy in charge of public health work is now free from administrative duties and can devote the whole of his time to hygiene; and that, generally, qualified guidance in hygiene work is available at all levels. It is considered that the system could with advantage be adopted in the smaller towns, with possible further extension. *R. Crawford*

1153. **Immediate Tasks of the Medical Services in Newly Developed Areas of the U.S.S.R.** (Медицинскую службу на целинных землях на уровень современных задач)
V. A. BARABOĬ. *Советское Здравоохранение* [*Sovetsk. Zdravookh.*] 17–21, No. 6, Nov.–Dec., 1956.

In the vast areas of Western Siberia, Altai, Kasazhstan, and Povolzh now being brought under cultivation the medical services for the new labour settlements are apparently causing some anxiety. The system of providing a small, 10- to 15-bed hospital for each collective labour settlement, often with no doctor in charge or one unsuited by recent qualification for independent work of this nature, away from all possibility of consultation with senior colleagues, has proved unsatisfactory in that the population prefers to seek a better standard of treatment in the larger town hospitals. The result is that the latter are overcrowded and that the small hospital, with a comparatively large staff, is rendered still less economical. The hygiene and sanitation of these new collective settlements also constitute a problem.

The recommendations here made are that the training of doctors should fit them more for this type of work; that wherever possible the small wards serving individual settlements should be combined into larger and more economical units, better equipped and better staffed, serving several settlements; that specialist skill should be more widely available; and that special hygiene staff should be provided, although the settlement doctor should be responsible for the hygiene of their areas.
R. Crawford

1154. **Problem Families: Their Discovery and Rehabilitation**
E. B. MEYRICK. *Royal Society for the Promotion of Health Journal* [*Roy. Soc. Prom. Hlth J.*] 77, 100–104, March, 1957.

1155. **Food Poisoning in Man, with Special Reference to Meat and Meat Products**
R. LOVELL. *Royal Society for the Promotion of Health Journal* [*Roy. Soc. Prom. Hlth J.*] 77, 85–91, March, 1957. 24 refs.

INDUSTRIAL MEDICINE

1156. Asbestosis with Pleural Calcification among Insulation Workers

J. FROST, J. GEORG, and P. F. MØLLER. *Danish Medical Bulletin* [*Dan. med. Bull.*] **3**, 202–204, Nov., 1956. 2 figs., 17 refs.

Experience in many countries has established that workmen employed in the lagging of pipes and boilers may contract pneumoconiosis in the course of their employment. Lagging materials vary in composition; common ingredients are kieselguhr, magnesia, and asbestos, and in more recent years rock wool and glass wool. About 100 laggers are employed in the shipyards and factories in and around Copenhagen. The authors examined 31 of these workmen who had been engaged for 20 years or more in the processes, and 9 were found to have definite signs of asbestosis. In addition, 19 showed abnormalities of the pleura, and in 11 of these there was calcification of the pleura, which was bilateral in 8 cases.

[The main purpose of the authors of this paper was to record the condition of " calcification " of the pleura in asbestos workers, they having found only one previous reference to such a case (Jacob and Bohlig, *Fortschr. Röntgenstr.*, 1955, **83**, 515). Since being shown this series of radiographs in Copenhagen in 1954, the abstracter has seen a series of similar radiographs from asbestos workers in the mines in South Africa. The dense, well-defined shadows are very striking, but as yet there is no necropsy evidence which confirms the deposition of calcium salts in the plaques. Since dense pleural sclerosis can simulate calcification such evidence of the morbid anatomy and pathology of the condition is needed.] *A. Meiklejohn*

1157. Cardiovascular Changes in Lead Workers. (Le alterazioni cardiovascolari nei lavoratori del piombo)

M. CREPET, F. GOBBATO, and G. SCANSETTI. *Minerva medica* [*Minerva med. (Torino)*] **2**, 1910–1918, Dec. 8, 1956. 6 figs., 37 refs.

The cardiovascular function of 73 persons employed for periods of 4 months to 54 years in work involving exposure to lead was investigated by routine clinical and electrocardiographic (ECG) examination at the Institute of Industrial Medicine of the University of Turin and the findings correlated with the results of laboratory tests which included a full blood examination and the estimation of porphyrins in the urine and blood and in some cases of urinary and blood lead content.

The workers were divided into three groups: (1) those showing signs of lead absorption but no toxic symptoms; (2) those suffering from or having just recovered from an acute attack of colic; and (3) those with a long history of exposure to lead, and with a past history of toxic symptoms. In Group 1 there were neither clinical nor ECG changes; in Group 2 the blood pressure was raised during the attack of colic, with either bradycardia or a tendency to tachycardia, and there was some evidence of vagal hypertonia; in Group 3 hypertension, with a diastolic pressure above 90 mm. Hg, was frequent, the ECG usually showed disturbance of rhythm, and there was one case of simple auriculo-ventricular block.

It is concluded that cardiovascular changes are significantly frequent in both acute and chronic lead poisoning. In the initial stages these changes are functional (arteriolar spasm) and therefore reversible; they are represented clinically by arterial hypertension, transitory at first, but leading eventually to changes in the renal, cerebral, and coronary circulation, of which coronary spasm in young persons is especially noteworthy. In the advanced stages of lead intoxication the arteriosclerotic changes become organic and irreversible. Of the cases here reported, 38·5% showed a constant hypertension, due in some to arteriosclerosis, in others to nephrosclerosis. Cardiac complications in the form of coronary disturbance or left ventricular insufficiency or both occurred in 21·2%. One case only of obliterating endarteritis (Buerger's disease) was observed. *Ethel Browning*

1158. The Bone Marrow in Occupational Lead Poisoning. (Il midollo osseo nell'intossicazione professionale da piombo)

V. PRATO and L. FIORINA. *Minerva medica* [*Minerva med. (Torino)*] **2**, 1937–1945, Dec. 8, 1956. 2 figs., 38 refs.

At the Institute of Industrial Medicine of the University of Turin stained films of the sternal bone marrow of 24 patients with lead poisoning were examined. The subjects were divided into three groups according to their clinical symptoms and length of exposure: (1) those who were not regarded as having reached the fully developed phase of poisoning, had had only short exposure, had suffered from fluctuating abdominal pain, and had no anaemia (7 patients); (2) those who had had acute episodic attacks (11 patients, all except 2 being anaemic); and (3) those with a history of long exposure and past episodes of intoxication (6 patients, of whom only one was anaemic, though all showed increased peripheral reticulocytosis).

In the great majority the erythroblastic activity of the bone marrow was more marked than the leucoblastic, the ratio being inverted in Group 2. The curve of erythrocytic maturation was characteristic of a stimulative effect, with a higher level of polychromatic than of orthochromatic erythroblasts. Karyokinesis was increased in Groups 1 and 2, and polyploidism (increase in the number of chromosomes) in Group 2, but not to such an extent as reported by other investigators. Erythroblasts with basophilic granulation were much more numerous in cases with severe anaemia, and in the more acute phases of intoxication.

Granulocytic haematopoiesis was generally unaltered. On the whole, except in Group 1, the reaction to lead intoxication in man appears to be stimulative, in contrast to that in animals, where it has been reported as aplastic. This stimulative effect is regarded as a proliferative reaction to an abnormal destruction of erythrocytes by lead, accompanied by increased rapidity of maturation. With the cessation or decrease of haemolysis, both these phenomena return to the normal, the erythroblastic reaction first. *Ethel Browning*

Forensic Medicine and Toxicology

1159. **Observations on Body Immersed in Water for Six Years**

W. LENTINO. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 1051–1052, Nov. 10, 1956. 4 refs.

The author describes the findings on examination of a body—that of a U.S. Army officer who had been shot by Italian partisans—which had been completely immersed in a fresh-water lake for 6 years. The partisans later confessed, and it was under their direction that the body was recovered. When first taken from the water the body was in a remarkable state of preservation, but decomposition set in very rapidly, the covering layers of the body disintegrating. [There appeared to be adipocere formation in all the subcutaneous tissues, but the description of this is not very convincing.] The presence of hair on the beard area and identification of the prostate established the sex, while examination of the bones indicated that the victim was just over 40 at the time of death. The body was identified as that of the officer from its height, the presence of a funnel deformity of the chest, the teeth, and the cause of death. The direction of transit of the bullets, which were found inside the skull, and the degree of penetration indicated that the wounds could not have been self-inflicted, and were not the result of point-blank discharges. The internal organs could be identified from their position and shape, but in none of them was it possible to identify any histological structure.

Gilbert Forbes

1160. **Post-mortem Persistence of Sex Chromatin**

A. D. DIXON and J. B. D. TORR. *Journal of Forensic Medicine* [*J. forensic Med.*] **3**, 161–168, Oct.–Dec., 1956. 4 figs., 6 refs.

Continuing their investigations at the University of Manchester into the medico-legal importance of sex determination by the examination of nuclear chromatin (*Nature* (*Lond.*), 1956, **178**, 797; *Abstracts of World Medicine*, 1957, **21**, 295), the authors have tested the survival of sex chromatin both in dissecting-room subjects and in full-term human foetuses—that is, in fixed and unfixed tissues.

The cadavers had been preserved for 10 to 12 months, and while scrapings from oral epithelium did not give satisfactory results, the sex of the individual could be correctly diagnosed in sections of facial skin, portions of the external ear, tongue, and mucoperiosteum of the hard palate. Sections from the fibro-elastic parts of the ear gave better definition of sex chromatin than the various epithelia. It was also clear in ear cartilage cells from two specimens used for teaching purposes which had been preserved for several years.

Tissues were then examined from human foetal limbs which had been placed in fresh water, exposed to the open air, put into a damp cellar, or wrapped in a cloth and placed behind a radiator to encourage mummification. Sex chromatin was discernible in all specimens up to the 15th day after death, disappearing first in the mummified tissue and remaining identifiable longest (23 days) in the limb placed in water. In unfixed tissue autolytic changes in cartilage cells were no less advanced than in other types of cell.

[Some excellent photomicrographs are reproduced in this paper.] *W. K. Dunscombe*

1161. **Morbid Anatomical Findings in Hypnotic Poisoning.** (Anatomische Befunde bei Schlafmittelvergiftung)

G. ADEBAHR. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **67**, 485–516, 1956. 12 figs., bibliography.

During the 7-year period 1948–55 149 fatal cases of poisoning by hypnotic drugs were investigated at the Institute of Forensic Medicine of the University of Cologne. In about one-third of these cases the subject had been found dead and the body sent for examination. In the other cases the period of unconsciousness between admission to hospital and death varied from 5 hours to 12 days, the average period being 3 days. The longest period of insensibility without concomitant pneumonia was 10 days. Men accounted for 67 cases, women for 82. The age incidence was greatest in men in the fifth and sixth decades, and in women between the third and fifth decades. Most fatalities resulted from the self-administration of barbitone, phenobarbitone, or cyclobarbitone for suicidal purposes. Occasionally, especially in patients taking cyclobarbitone, alcohol or morphine derivatives contributed to the cause of death. Accidental overdosage was rare.

A comprehensive histological examination, including the brain, was made in all cases and detailed accounts of 3 illustrative cases are given. The most characteristic lesions were found in the basal ganglia of the brain. Here there was a massive, symmetrical necrosis of the globus pallidus with a strong glial reaction. In the thalamus and claustrum there were localized foci of softening. Other areas of the brain involved were the paraventricular nuclei and the nucleus supraopticus. In these areas there was severe oedema of the tissues and degeneration of nerve cells, as demonstrated by pyknotic nuclei, clumping of Nissl granules, and karyolysis. In just over half the cases skin lesions were present. These consisted of severe primary vesicular eruptions with secondary necrotic changes. In 2 cases there was necrosis of the tubules of the kidney.

[This is an important paper which should be read in the original. The extensive bibliography (which occupies nearly 7 pages) will be of much value to those who are working on, or interested in, the effects of barbiturate poisoning.] *Ruby O. Stern*

Anaesthetics

1162. **Suxamethonium and Respiration. Investigation of a Possible Central Action of Suxamethonium Chloride during Clinical Anaesthesia**
L. T. Rees and M. H. A. Davidson. *Anaesthesia* [*Anaesthesia*] **12**, 57–60, Jan., 1957. 3 figs., 2 refs.

Suxamethonium, being a muscle relaxant, necessarily suppresses the movements of the respiratory muscles. To determine whether breathing is also interfered with by a direct effect of the drug on the respiratory centre it is necessary to free the patient from the physiological consequences of muscular weakness and to protect the centre from changes in *p*H and in the carbon dioxide and oxygen levels in the blood. At the Royal Infirmary, Newcastle upon Tyne, the authors devised an apparatus which produced a standard, adequate inflation of the lungs for each attempt—however weak—at inspiration. Thus with subparalysant doses of suxamethonium regular respiration was maintained despite the weakness of the respiratory muscles and, since the rate of respiration was controlled by the patient, without change in the levels of the blood gases. In these circumstances any change in the respiratory rate following an injection of suxamethonium would have to be ascribed to a direct effect of this compound on the central nervous system. Pethidine was given as a control and an effect on respiration was clearly shown. Suxamethonium, however, had no effect. It is emphasized that the dosage used was not maximal, as complete paralysis would of course have made the experiment impossible.

H. Lehmann

1163. **Exacerbation of Pre-existing Neurologic Disease after Spinal Anesthesia**
L. D. Vandam and R. D. Dripps. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 843–849, Nov. 1, 1956. 28 refs.

A long-term follow-up study of 10,098 patients who received spinal analgesia at the Hospital of the University of Pennsylvania showed that in 11 there was post-operative exacerbation of pre-existing neurological disease. In one patient a previously symptomless spinal meningioma was discovered and in 2 others metastatic deposits in the spine were found after spinal analgesia. It is pointed out that the resulting symptoms and igns might well be attributed to the spinal analgesic and the true diagnosis be delayed. In other cases spinal analgesics given some time after herpes, encephalitis, and degenerative disease of the central nervous system caused a recrudescence of symptoms. In patients with backache, diabetes, or peripheral neuritis postoperative neurological symptoms were confused with complications of spinal analgesia.

The authors conclude that this form of analgesia should be avoided in patients giving a history of any form of neurological disease. *Mark Swerdlow*

1164. **Measurement of the Depth of Barbiturate Narcosis**
A. Forbes, J. K. Merlis, G. F. Henriksen, S. Burleigh, J. H. Jiusto, and G. L. Merlis. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 541–558, Nov., 1956. 13 figs., 24 refs.

The authors, working at the National Veterans Epilepsy Center (Harvard University), Boston, have studied the effects of varying levels of narcosis induced in 72 cats and one monkey with pentobarbitone sodium given initially to all but 11 cats in a dose of 45 mg. per kg. body weight intraperitoneally, subsequent automatic control of the anaesthesia being obtained by means of an intravenous injection device which was electrically actuated through the negative feed-back system by the rectified and integrated electrical energy derived from the electroencephalogram (EEG), the latter being obtained by means of steel gramophone needles inserted into the animal's skull. Respiration was also recorded electrically, body temperature was kept at a constant level (35° or 39° C.), the presence or absence of the flexion reflex evoked by pinching a toe-pad with forceps was recorded frequently, and the blood barbiturate level was estimated spectrophotometrically, while the blood pCO_2 in mm. Hg was calculated from the carbon dioxide concentration in many cases. Frequent counts of the brain waves were made by counting the number of waves which exceeded one-third of the maximum observed potential during a 40-second stretch of the EEG recording.

It was shown that the vigour of the flexion reflex indicated the depth of narcosis in the lighter stages, but that the reflex disappeared as narcosis deepened. The brain-wave count gave a sensitive indication of the depth of narcosis and showed a close correlation with the blood barbiturate level, this count being more reliable than the respiratory rate or the recorded electrical energy derived from the EEG. Narcosis was augmented by increased carbon dioxide tension in the blood, but was much reduced when the body temperature was allowed to rise.

In the monkey the general results were similar, except that the brain-wave count was lower and in deep narcosis the waves came in bursts instead of singly. The authors propose a new technique for the automatic regulation of intravenous injection of barbiturate by means of a triggering device which would take into account not only the integrated electrical energy of the EEG but also the brain-wave count.

[Readers interested in details of this technique are advised to consult the original paper.]

John N. Walton

1165. **Hypothermia by Internal Cooling**
H. H. Khalil. *Lancet* [*Lancet*] **1**, 185–188, Jan. 26, 1957. 4 figs., 10 refs.

Radiology

1166. **Haemolytic Action of Radiations: Research on the Part Played by Destruction of Circulating Erythrocytes in the Genesis of *X*-ray Anaemia.** (Azione emolitica delle radiazioni: ricerca sull'eventuale compartecipazione della distruzione di globuli rossi circolanti nella genesi dell'anemia da raggi X)
L. GHIRINGHELLI. *Medicina del lavoro* [*Med. d. Lavoro*) **47**, 562–570, Oct., 1956. 4 figs., bibliography.

According to the author, although exposure to *x* rays causes an abnormal destruction of erythrocytes, it is not certain whether *x* rays have any direct effect on circulating erythrocytes. In the hope of providing clarification he therefore carried out 3 series of experiments.

In the first series the fate of the erythrocytes in samples of blood removed from experimental animals, irradiated, and then re-injected slowly into the same animals was determined.

Guinea-pigs varying in weight from 360 to 480 g. were used, and blood amounting to one-quarter to one-third of the total circulating volume (10 to 15 ml.) was removed by intracardiac puncture, heparinized, placed in a sterile tube, and irradiated with doses of *x* rays varying from 500 to 4,000 r. Immediately after irradiation it was re-injected very slowly into the jugular vein. All the animals stood the procedure well. Estimation of the haemoglobin concentration, erythrocyte count, reticulocyte count, and haematocrit value was carried out before and 1, 3, 5, 10, and 20 days after the operation. No change worthy of note was found in the blood picture of any of the animals.

In the second series samples of heparinized human blood were diluted to 1% with normal saline at *p*H 6·8, placed in special paraffin cells, and irradiated with doses varying between 500 and 6,000 r. After irradiation the suspensions were left at room temperature for 24 hours to see if there was any change in cell-wall permeability and then placed in Wassermann tubes, heated to 53° C. for various periods, cooled, centrifuged, and the supernatant examined spectrophotometrically. The degree of haemolysis found was proportionate to the dosage of *x* rays and also to the duration of heating. Control suspensions heated for the same periods but not irradiated did not show evident haemolysis.

In the third group of experiments heparinized human blood was again diluted as above and irradiated with similar doses. Immediately afterwards, the erythrocytes were haemolysed, streaked on a coverslip, and examined under the electron microscope after shading with gold. In general the appearances were similar to those of normal blood, but in samples given 4,000 r craters were found more frequently and also the special formations called *haematexodies* by French writers. These appeared as filaments with swollen extremities or as spherical granules, either free or attached to the erythrocytes.

The author concludes that within the range of *x*-ray dosage employed by him mature erythrocytes possess a notable degree of radioresistance, and that their destruction is impossible in patients even when heavy doses of *x* rays are given. *W. K. Dunscombe*

1167. **The Incidence of Leukaemia in Ankylosing Spondylitis Treated with *X* Rays**
J. D. ABBATT and A. J. LEA. *Lancet* [*Lancet*] **2**, 1317–1320, Dec. 29, 1956. 13 refs.

The records of two series of cases of ankylosing spondylitis from the Ministry of Pensions and National Insurance have been examined. One of these series, of 1,627 men, had been treated by radiotherapy; the other, of 399 men, had not been irradiated but had been treated by other methods. The expected deaths from leukaemia have been calculated and compared with those actually observed. In the non-irradiated series 0·17 death was expected and none observed, a very good agreement between expectation and observation. In the irradiated series 0·33 death was expected and 7 were observed. The odds against this excess of deaths being due to chance were greater than 1,000,000 to 1. It has been established that leukaemia is associated with (1) ankylosing spondylitis, or (2) irradiation, or (3) ankylosing spondylitis treated by irradiation.

The hypothesis that irradiation was the sole cause of the leukaemia was tested, but the data were insufficient to provide a firm answer. It is hoped to obtain a larger series of non-irradiated individuals by using information from the 1914–18 war, which may make possible a final decision on the exact rôle of irradiation. The data in this survey have been discussed in the light of other independent evidence. It has been concluded that irradiation plays the main part in the production of the observed cases of leukaemia.—[Authors' summary.]

1168. **Intracavitary Administration of Radioactive Colloidal Gold (Au^{198}) for the Treatment of Malignant Effusions. A Report of Thirty-one Cases and an Appraisal of Results**
M. P. OSBORNE and B. E. COPELAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 1122–1128, Dec. 13, 1956. 2 figs., 18 refs.

The authors evaluate the results in 31 consecutive cases of malignant peritoneal or pleural effusion treated with radioactive colloidal gold (^{198}Au) at the New England Deaconess Hospital, Boston, since 1951. The physical and biological properties of colloidal ^{198}Au are reviewed, and the rate of decay and distribution of radioactivity in the fluid and surrounding tissue, as well as the estimated amount of fluid remaining—which were determined experimentally in one case by daily withdrawal of samples of fluid—are shown graphically.

Tables showing details of each case, such as pathological diagnosis, medical history, treatment, period of survival, and result, are presented. In the 14 cases of

pleural effusion treated the dose of ^{198}Au ranged from 69 to 106 mc. The fact that 11 of these patients were female and 3 male reflects, in the authors' opinion, the high incidence of serous spread from tumours of the breast and ovary. Assessment of the results showed that benefit was obtained in 8 cases, no benefit in 2, and the remaining 4 cases were considered indeterminate since the patients died within 3 weeks of treatment. Of the 17 cases of peritoneal effusion, which were treated with doses of ^{198}Au ranging from 87 to 107 mc., and in all but one of which malignant cells were found in the effusion, complete control of the ascites was achieved in 2 cases, doubtful benefit was obtained in 3, no benefit in 7, and the remaining 5 cases were assessed as "indeterminate".

The authors consider it noteworthy that no case of radiation sickness occurred, and also that, with the exception of patients previously treated, malignant cells were found in the fluid in all cases. While admitting the smallness of the series they report that they could find no prognostic significance in the type of tumour or the length of history. They conclude that the ideal patient for this type of therapy is one who is not severely debilitated and in whom the chief problem is the accumulation of fluid. *E. D. Jones*

1169. **Carcinoma of Larynx. Results of Roentgen Therapy during a Period of Fifteen Years (1937–1952)**
E. L. JENKINSON, L. KAO, P. H. HOLINGER, K. C. JOHNSTON, and R. W. DONNELLY. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **76**, 942–948, Nov., 1956. 1 fig., 6 refs.

Between 1937 and 1952 at St. Luke's Hospital, Chicago, 119 cases of carcinoma of the larynx were treated by *x*-irradiation, and in this paper the results obtained in 109 are reviewed, including 27 with recurrence after treatment at other hospitals—irradiation in 4 and surgery in 23. There were 93 males and 16 females, and the average age was 59·2 years. The cases are classified according to four clinical stages and subdivided into those with intrinsic and those with extrinsic laryngeal lesions. Of the 109 cases, 68 were in Stage IV—that is, more than half were late cases. In 20 cases the patient was either lost to follow-up or died from other causes in the first 5 years. At the time this paper was written 30 patients were alive and well.

In the group of 28 cases with intrinsic lesions there were 17 successes, and in the group of 61 cases with extrinsic lesions the successes numbered 13. When the results were broken down according to the stage of the disease it was seen that treatment was successful in 11 out of 14 cases in Stage I, 2 out of 4 in Stage II, 7 out of 17 in Stage III, and 10 out of 54 in Stage IV.

The technique employed consisted in two opposing lateral fields, 140r in air being given daily to each to a total of 3,780 r in 4 to 5 weeks. The minimum depth dose was 4,700 r and the skin dose 5,500 r. The tube characteristics were 200 kV constant potential, 10 mA, a Thoreus-II filter with a half-value layer of 2 mm. copper. The usual size of field was an 8-cm. diameter circle. A moist desquamation of the skin was noted in the majority of patients in the fourth week, but cleared up within 2 months of completion of treatment. In 13 cases tracheotomy had to be performed, during treatment in 2 and subsequently because of oedema in 11.

The authors conclude that the site and extent of the lesions are of the utmost importance in prognosis, and stress the value of early diagnosis, particularly in patients with extrinsic lesions. *D. Pearson*

1170. **Squamous Cell Carcinoma of the Thoracic Esophagus. An Evaluation of Treatment Methods**
H. W. BURNETT and S. W. MOORE. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **76**, 949–955, Nov., 1956. 4 figs., 14 refs.

The authors have attempted an evaluation of the various methods of treatment of squamous-celled carcinoma of the oesophagus based on their findings in all histologically proved cases seen in clinics of the New York Hospital between 1940 and 1950.

Of 64 patients in whom squamous-celled carcinoma of the thoracic oesophagus was diagnosed during this period, 10 had evidence of distant metastases and were not included in the study. Radical surgery was first considered for the other 54, but only 39 underwent thoracotomy, and of these, only 17 were subjected to complete resection, the condition in 22 being found to be inoperable. There were 7 operative deaths after resection and 2 after thoracotomy alone.

Altogether 28 patients were referred for *x*-ray therapy, including those whose condition was not considered suitable for surgery or was found to be inoperable at thoracotomy, a conventional 250-kV apparatus and a beam-directed technique with three anterior and three posterior portals being used. In this group there were no hospital deaths, but only 11 of the patients were able to complete the course of irradiation of 4,500 r or more to the tumour in 5 to 6 weeks.

Of the 39 patients subjected to thoracotomy, 3 were alive 3 years afterwards; of the 28 receiving irradiation, one survived at 3 years, a proportion of one out of 11 who completed the course.

Diagrams are reproduced which show that in the irradiated group the percentage of survivors in the first 12 months was higher than in the surgically treated groups. They also show that among the patients who completed the course of *x*-ray therapy the percentage survivals at all stages were as good as or better than in the surgical group. The authors consider that the over-all survival rate and the palliation achieved could be much improved if all cases of squamous-celled carcinoma of the oesophagus were treated primarily by adequate irradiation, without preliminary thoracotomy. *D. Pearson*

1171. **Studies of the Effect of *X*-radiation on 24-hour Variations in the Mitotic Activity in Human Malignant Tumours.** [In English]
E. TÄHTI. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] Suppl. 117, 1–61, 1956. 40 figs., bibliography.

History of Medicine

1172. **The Professional Ethics of the Greek Physician**
L. EDELSTEIN. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **30**, 391–419, Sept.–Oct., 1956. Bibliography.

In this extended form of the William Osler Lecture delivered at Montreal General Hospital in December, 1955, the author outlines the various ethical positions taken by ancient physicians and discusses the origin of the concept that medicine itself imposes certain obligations on the physician.

At first glance it would appear that the ethic of philanthropy was already securely established in the Classical Age of Greece; but the author seeks to show that in fact this was not so. The early Hippocratic books offered rules which, if the physician chose to accept them, established a set of values governing treatment and gave a personal pledge of safety to the patient. At this time physicians were itinerant craftsmen, taught by craftsmen-physicians, practising without a licence, and judged on skill alone. Medicine was unaffected by moral considerations. However, from the latter half of the 4th century B.C., following a revaluation of the arts and crafts, there was a change in the ethics of the medical craftsman in accordance with various systems of philosophy. Further, the medical craft slowly developed into a science. In this new age the moral issues of medical practice were discussed, and questions of medical ethics answered from different philosophical points of view. The physician's ethics became identified with those of the philosophical school to which he belonged. Further, the Hippocratic Oath, originally a literary manifesto, was not taken by all physicians, if indeed it was taken at all before the end of antiquity. As of old, moral obligations were accepted voluntarily. The various outlooks adopted by the craftsmen-physicians and the scientist-physicians during this second stage of ethical development are discussed.

Galen, on the other hand, required only that the physician should be an expert in medicine; but this is not to say that the ancients never identified medicine with a love of humanity. That there was a clear realization some 100 years previously of a medical humanism inherent in the task of the physician is borne out by the writings of Scribonius Largus, who was able to find his philosophy, at the best, only by implication in the Hippocratic writings. However, he was probably not the originator of such an attitude, which the author finds reminiscent " of the Stoic philosophy of humanism evolved in the 2nd century B.C. by Panaetius and embedded in Cicero's book *On Duties* " which, he thinks, may have had a common source. The few existing testimonies concerning strictly professional ethics in this later period are discussed.

Medical humanism does not appear to extend beyond A.D. 350, probably because Stoic philosophy waned about that time. Subsequently, the Neo-Platonists established Galen as the unchallenged authority in medicine; through him the philosophical ethics of the scientist-physician came to predominate.

L. G. Fallows

1173. **John and George Armstrong**
H. P. TAIT. *Scottish Medical Journal* [*Scot. med. J.*] **2**, 42–45, Jan., 1957. 6 refs.

It was in the field of child care that the two Armstrong brothers, John and George, made their pioneer contributions. John graduated at Edinburgh in 1732, and 3 years later published anonymously an " Essay for Abridging the Study of Physick ", in which he castigated the charlatans. In 1737 " A Synopsis of the History and Cure of Venereal Diseases " appeared under his own name, and in 1742 an anonymous anthology on children's diseases, " A Full View ", was published, which is now ascribed to him. In " The Art of Preserving Health " (1744) he commended a temperate life and extolled the virtues of fresh air, pure drinking water, and healthful exercise. He became physician to Duke's Hospital, London, in 1746 and to the Army in 1760. His " Medical Essays ", in which he again attacked the incompetence of his professional brethren, appeared in 1773. He died on September 7, 1779. His younger brother, George, is noteworthy as the founder of the Dispensary for the Infant Poor, opened in London on April 24, 1769, the first charitable institution of its kind. He had joined his brother in London in 1746 and helped in his practice, although he left Edinburgh without graduating. His observations on children contained in his " Essay " (1767) were the results of his own experience, including the rearing of three daughters; this work ran into several editions. In 1777 he noted the familial incidence of congenital pyloric stenosis. He helped to rationalize artificial feeding, and he anticipated the modern health visitor by advocating " proper assistants to visit at their own homes such poor children as are not in a condition to be brought out". In 1769, with the idea of the dispensary in mind, he wrote: " If you take away a sick child from its parents or nurse you break its heart immediately: and if there must be a nurse to each child, what kind of hospital must there be to contain any number of them? " [criticisms which are still commonplace today]. In 1781 George Armstrong suffered a stroke, and the dispensary had to close down. During its existence 35,000 children had been treated, patients coming from " most of the villages within 8 to 10 miles of London ". He died in London in 1789, but his burial place remains unknown.

I. M. Librach

1174. **John Hunter and Veterinary Medicine**
E. A. GRAY. *Medical History* [*Med. Hist.*] **1**, 38–50, Jan., 1957. 9 refs.